Obstructive sleep apnea in bariatric surgery

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VRIJE UNIVERSITEIT

Obstructive sleep apnea in bariatric surgery

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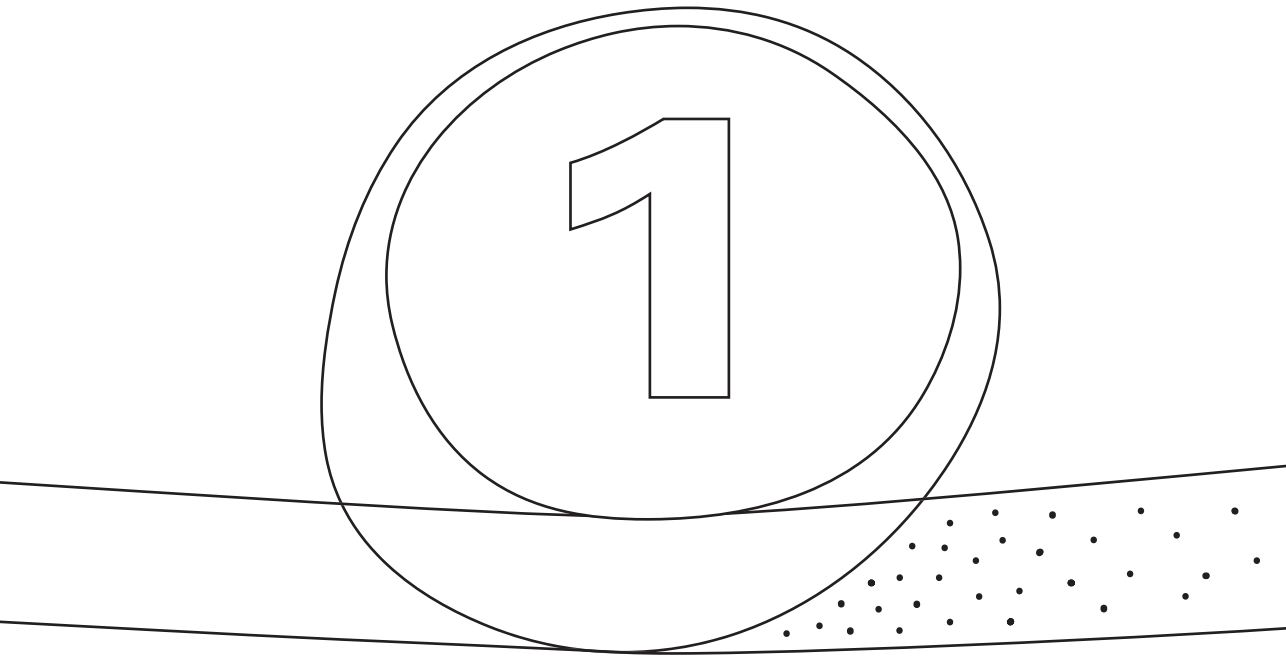
General introduction and outline of thesis



GENERAL INTRODUCTION

Obesity, once a sign of health and welfare, is now considered a multi-organ, potentially fatal disease. The continuous rise of obesity numbers has caught the attention of many health organizations and is one of todays greatest world concerns.

Thousands of years ago, people travelled across land in search of water and food. The body was designed to store fat when food was available and utilize it in times of need. It was an ongoing process of weight gain and loss. Drastic environmental and lifestyle changes have ignored this physiological principle and introduced a new phenomenon in 1950s, the obesity epidemic[1]. The basis for this epidemic is the abundance of food along with the arise of supermarkets, restaurants and fast-food industries, bigger portion sizes, increased amounts of sugar and competitive prices for unhealthy food. Fast food industries in the USA have increased from 30,000 in 1970 to more than 233,000 in 2004 and the daily intake of kilocalories worldwide has increased with 600 kilocalories per day in the last 50 years[2]. Introduction of daytime television, microwaves and drive-through restaurants have changed eating behaviors negatively; eating in front of the television or on the road have become common practice. Humans are overeating and physical activity is almost out of our vocabulary. A quarter of the worlds adults do not exercise enough due to television, computers and a lack of cycle cultures, sport- and recreation facilities contribute to this decreased exercise[3]. A caloric imbalance caused by increased consumed and decreased expended calories is the fundamental cause of obesity.

OBESITY – DEFINITION AND PREVALENCE

Obesity represents a certain amount of excessive adipose tissue, negatively affecting health status, life expectancy and operative outcome. The exact definition is formulated with the body mass index (BMI), a ratio of weight in relation to length. It can be calculated by dividing someone's weight in kilograms by his or her height in meters squared (kg/m^2) and enables us to categorize a person as underweight, normal weight, overweight, obese, morbidly obese or super obese, **Table 1**. Obesity is defined as a BMI ≥ 30 kg/m^2. The basis of the BMI was formulated by Adolphe Quetelet between 1830 and 1850 when interest in an index measuring weight came with increasing obesity[4]. Due to its simplicity, the BMI has become a universally used metric for weight.

Table 1 - Body Mass Index and weight categories

Body Mass Index (kg/m^2)	Weight category
< 18	Underweight
18-24.9	Normal weight
25-29.9	Overweight
30-34.9	Obesity
35-49.9	Morbid obesity
≥ 50	Super obesity

The overall global population is progressively affected by obesity. Except for parts of sub-Saharan Africa and Asia, all regions include more individuals with obesity than underweight[5]. Worldwide, the prevalence in adults increased from 5% in 1980 to 13% in 2014, **Figure 1**[5]. This equates to 641 million obese adults; 266 million men (41.5%) and 375 million women (58.5%).

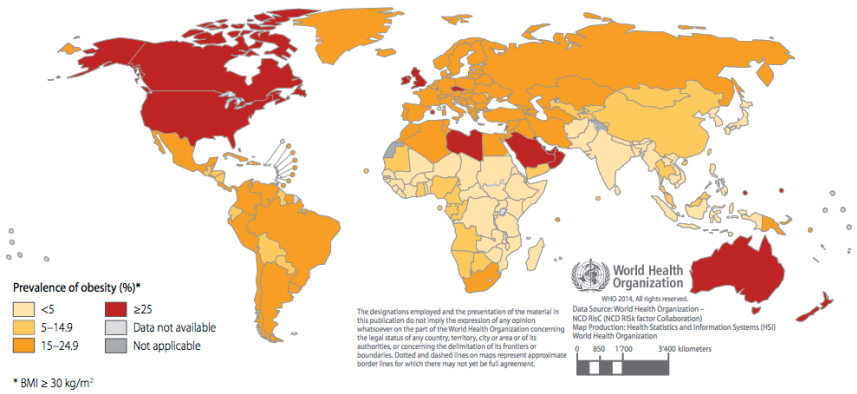


Figure 1 - Prevalence of obesity worldwide in 2014
Source: World Health Organization, www.who.int

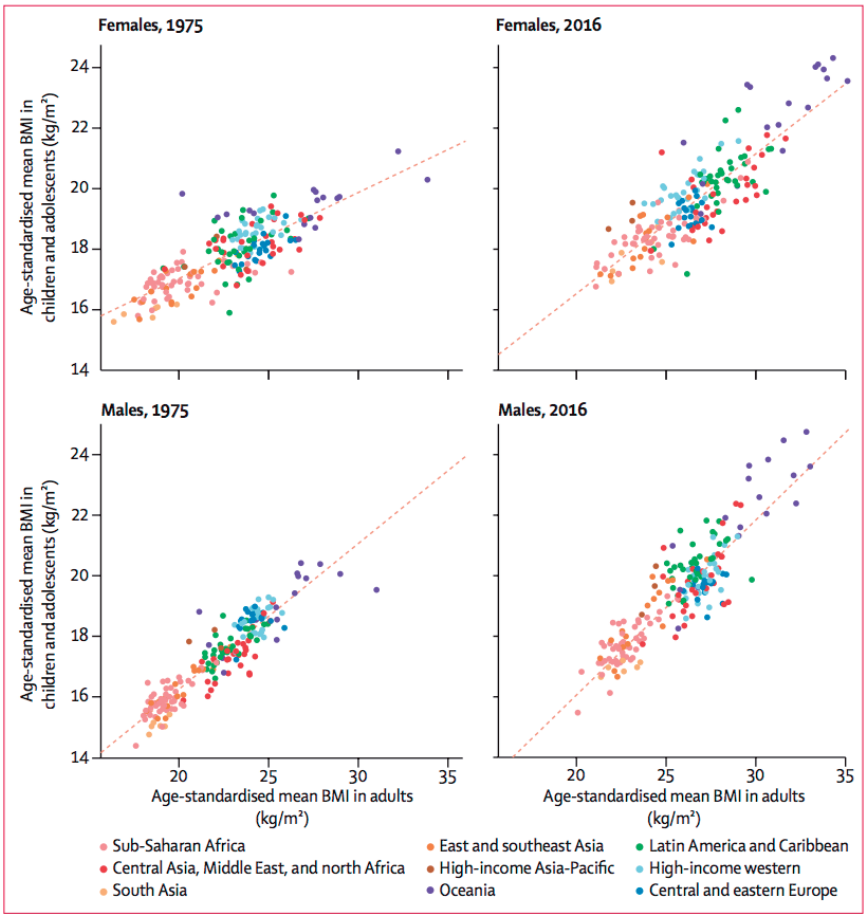


Figure 2 - Comparison of mean BMI in children, adolescents and in adults
Children and adolescents were aged 5-19 years and adults were aged 20 years and older. Each point shows one county. The dotted line shows the linear association between the two outcomes. BMI = Body Mass Index
Source: Lancet 2017; 390: 2627–42

Global obesity rates have always been higher in women, but tripled in men and doubled in women, Figure 2[6]. In the period 1975 to 2014, obesity rates among men increased from 3.2% to 10.8%, and among women from 6.4% to 14.9%[6]. By the year 2030, the number of obese US adults is expected to rise to 40-50%[6]. Knowing that obesity causes multi-organ diseases and decreased life expectancy, this is a threatening perspective for global health.

METABOLIC AND BARIATRIC SURGERY

Billions of dollars are spent on conservative weight loss programs to tackle the problem of obesity every year. Failure of long term results have led to a more aggressive approach, including bariatric- or also known as metabolic surgery. This term has been derived from the Greek words baros (weight) and iatros (doctor) and refers to the surgical treatment of obesity. The jejunoileal bypass, in which most of the intestines were bypassed and the stomach kept intact, was the first performed weight loss procedure in the 1950s[7]. Adverse outcomes of diarrhea and severe vitamin deficiencies forced surgeons to search for alternatives. Observed weight loss among patients undergoing partial stomach removal from ulcers was the onset of a historical moment in bariatric surgery. In the 1960s, Dr. Mason and Dr. Ito performed the first gastric bypass, characterized by restricting the amount of food by reducing the stomach and causing malabsorption of nutrients through bypassing the small intestines[7]. Over the past decades the gastric bypass has been modified to its current form, the Roux-en-Y gastric bypass (RYGB). It is considered the gold standard and is competing popularity with the sleeve gastrectomy. Other popular but less performed procedures are the historically most performed but now almost abandoned Swedish adjustable gastric banding, highly effective but problematic malabsorption giving duodenal switch, and the upcoming one anastomosis gastric bypass.

Open bariatric surgical procedures have been converted to minimally invasive with the introduction of laparoscopic surgery[8]. Improved perioperative recovery and outcome in terms of complications, weight loss, comorbidities, quality of life and life expectancy resulted in a growing interest in bariatric surgery. Reimbursement by insurance companies allowed a growth from 150,000 procedures in 2002 to almost 700,000 in 2016[9,10].

Criteria for bariatric surgery were set at the National Institutes of Health consensus conference in 1991[11]. Patients are candidates for bariatric surgery if they are morbidly obese, had failed conservative therapies such as diets and exercise programs, are motivated to change their lifestyle and have no significant psychological diseases. The International Federation for the Surgery of Obesity and metabolic disorders (IFSO) added the criteria age between 18 and 65 years, no drug dependency problems and no pregnancy anticipation in the first two years after surgery[12].

BARIATRIC SURGERY AND OBSTRUCTIVE SLEEP APNEA

Excessive adipose tissue negatively affects the function of organ systems. Anatomical, cardiovascular, metabolic, neuromuscular and hormonal changes all occur due to obesity. Many of these changes are associated with the presence of obstructive sleep apnea (OSA), affecting more obese individuals than type II diabetes, hypertension and dyslipidemia[13]. OSA in obese individuals has been unrecognized for many years, but its complex pathophysiology, high prevalence and related health risks have resulted in a rising interest and performance of research in this field.

OSA is the most prevalent sleep disordered associated breathing problem and is characterized by obstruction of the upper airway followed by blockage of airflow and oxygenation in the lungs. The average number of apneas (complete collapse) and hypopneas (partial collapse) per hour of sleep forms the apnea-hypopnea-index (AHI), indicating the severity of OSA. A few breathing stops per hour (<5) is considered normal. An AHI of 5-15/hour is considered mild OSA, an AHI of 15-30/hour moderate OSA and more than 30 events/hour severe OSA.[14]

OSA only occurs during sleep and is accompanied with loud snoring and breathing stops. Severe daytime sleepiness, morning headache, dry mouth, less intellectual performance and sexual dysfunction are OSA related daytime complaints. Untreated OSA predisposes to high blood pressure, cardiovascular events e.g. myocardial infarction and stroke, some types of cancer, and weight gain due to metabolic and hormonal changes and decreased physical activity due to tiredness. OSA results in an increased risk of traffic, domestic and home accidents, as well as an increased perioperative risk of severe desaturations and cardiopulmonary complications.

The pathogenesis of OSA is multifactorial and complex. Local anatomy, obesity, gender, age, sleep position and sedative drugs are examples of risk factors for OSA and its severity[13]. The prevalence of OSA increases with BMI and age and is more common in men than women. Around 2% and 4% of middle aged women and men respectively suffer from OSA in the general population. In morbidly obese individuals, the prevalence increases up to 70%[15]. One of the hypothesis explaining obesity as an important risk factor for OSA is that fat deposition results in diminished pharyngeal airway size, thereby increasing the risk of apneas.

Diagnosing definitive OSA requires a sleep study, of which the gold standard is a polysomnography (PSG)[14]. Validated screening questionnaires have been developed for the general population. The majority of questions is related to both OSA and obesity, decreasing the ability to differentiate participants on their OSA status in the bariatric population. This suggests that usage of standard screening questionnaires is even more inferior to sleep studies in the bariatric population. OSA can be treated with life style changes, devices and surgery. The most commonly used and in most countries reimbursed treatment is continuous positive airway pressure (CPAP), a device providing positive pressure in the upper airway preventing its collapse[14].

Morbid obesity and OSA are independent risk factors for perioperative complications. A combination of both suggests that special attention should be paid on the recognition and anticipation of OSA in bariatric surgery to prevent disastrous perioperative complications.

In this thesis, we aim to gain more knowledge regarding the perioperative management and outcome of OSA patients undergoing bariatric surgery.

RESEARCH QUESTIONS

Several studies with small sample sizes have shown a high prevalence of OSA in the bariatric population. The objectives of chapter 2 are to determine the prevalence of OSA with respect to the different severity levels and postoperative OSA related outcomes in a large cohort in which all bariatric patients undergo mandatory sleep studies and individualized OSA care.

Performing mandatory PSG in all bariatric patients has been a challenging task for most bariatric centers. Along with increasing numbers of bariatric procedures, centers are facing a lack of PSG capacity, strict time schedules to surgery and high costs. With the aim to search for alternatives, chapter 3 and 4 outline the value of venous derived biomarkers and the validation of a simple sleep monitor respectively by comparing results with the PSG.

Reducing OSA related complications is the main reason to diagnose OSA. To evaluate the effect of OSA diagnosis, chapter 5 provides an overview of the literature on post-bariatric cardiopulmonary complications and its association with OSA. In most cases, mild OSA patients are not treated with CPAP. In chapter 6 it is evaluated whether presence of positional OSA in these patients would change indication for CPAP therapy.

CPAP is provided in approximately one-third of bariatric patients. Concern exists that the continuous provided pressure predisposes to mechanical stress of the suture lines by not only reaching the upper airway, but also the esophagus and stomach. Chapter 7 focusses on the association of perioperative CPAP usage and suture line disruption, being the most feared complication of bariatric surgery.

Bariatric outcomes include postoperative complications, weight loss, comorbidity- and quality of life improvement. Knowing OSA goes along with daytime symptoms, metabolic, cardiovascular and hormonal changes, it could be hypothesized that bariatric outcomes may negatively be influenced by OSA. Chapters 8, 9 and 10 aim to assess whether OSA is a predictive factor for postoperative complications, insufficient weight loss and decreased quality of life respectively. Chapter 11 describes the success rates of bariatric surgery regarding OSA severity.

Bariatric centers follow their own OSA protocols due to limited literature and a rapid increase of bariatric surgical procedures. Chapter 12 outlines a consensus based guideline on the perioperative management of OSA in a bariatric specific population. Chapter 13 is a summary and update of chapter 12, one year after publication.

Chapter 14 provides discussion and future perspectives, folllowed by a summary of this thesis in chapter 15.

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Value of routine polysomnography in bariatric surgery

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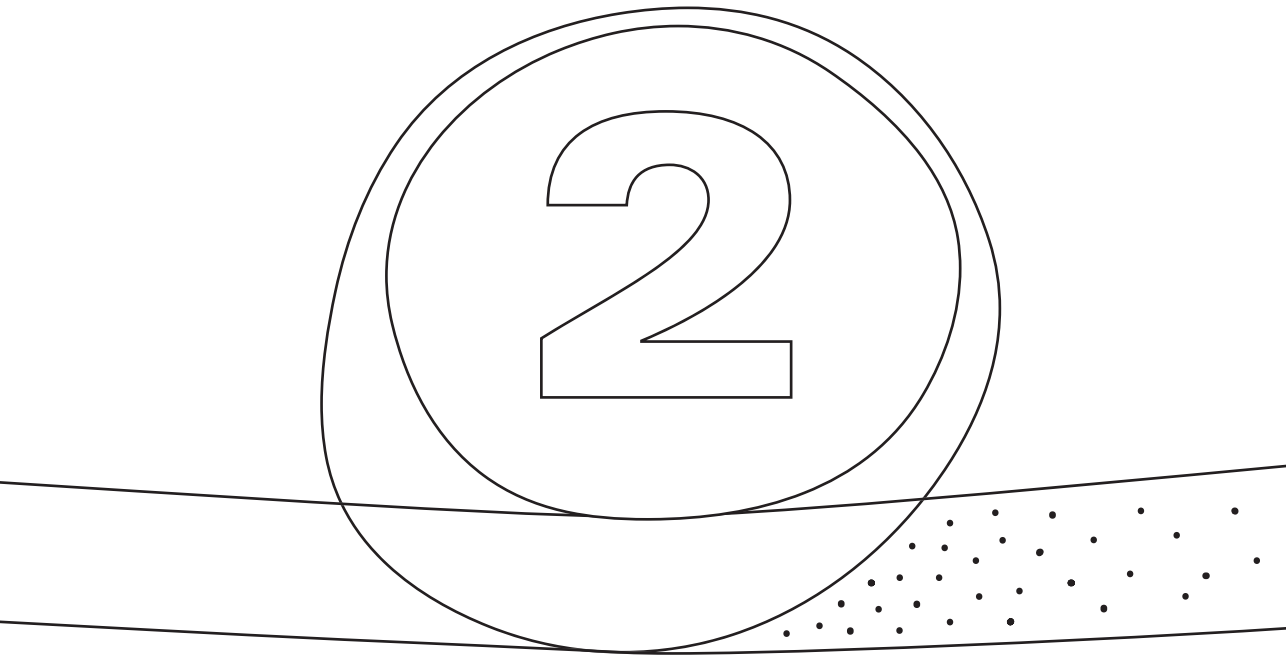

ABSTRACT

Introduction: Obstructive sleep apnea (OSA), present in 60-70% of bariatric surgery patients, is a potentially life-threatening condition when not detected and managed appropriately. The best available method to identify the severity of OSA is polysomnography (PSG). However, routine PSG measurements have not been accepted as standard modality in bariatric surgery. We report our experience with routine poly(somno)graphy (P(S)G) in a cohort of patients undergoing bariatric surgery to assess the true prevalence of OSA with respect to the different severity levels as determined by the apnea-hypopnea-index (AHI).

Methods: AHI data were retrospectively collected from all patients who underwent bariatric surgery from 2012 onwards, when the performance of preoperative P(S)G became mandatory. Mild, moderate and severe OSA were defined as an AHI ≥ 5/hour, ≥ 15/hour and ≥ 30/hour respectively. Prevalence and Number Needed to Screen (NNS) were calculated for all OSA severity levels.

Results: A total of 1358 patients were included. OSA was detected in 813 (59.9%; NNS: 2) patients. Moreover, 405 (29.8%; NNS: 4) patients were diagnosed with an AHI ≥ 15/hour and 213 (15.7%; NNS: 7) with severe OSA (AHI ≥ 30/hour). Extreme AHI thresholds of ≥ 60/hour and ≥ 90/hour were detected in 79 (5.8%; NNS: 18) and 17 (1.3%; NNS: 77) patients respectively.

Conclusion: One-third of the bariatric surgery patients have an AHI ≥ 15/hour and would benefit of Continuous Positive Airway Pressure therapy. In order to increase perioperative safety and avoid the preventable risk of perioperative complications, we recommend mandatory P(S)G prior to bariatric surgery.

INTRODUCTION

Obstructive sleep apnea (OSA), the most common form of sleep apnea caused by repetitive upper airway obstruction, occurs in 2-4% of the general population[1]. Older age, male gender and obesity predispose to OSA. In 60-70% of individuals with a Body Mass Index (BMI) greater than 35 kg/m^2, OSA is present[2-3]. Accompanying symptoms include sleepiness (increasing the risk of traffic accidents), weariness and neurocognitive disorders. Untreated OSA is associated with long-term cardiovascular (CV), pulmonary and neurovascular risks such as hypertension, myocardial infarction, respiratory failure and death[4-6]. Additionally, two recent meta-analyses showed that OSA patients developed more cardiac events, respiratory failure and desaturations post-surgery[7-8].

Identifying OSA is difficult as clinical symptoms, medical history and standardized questionnaires, either combined with or without neck circumference or BMI, have failed to determine the presence of OSA accurately[3;9]. Polysomnography (PSG), measuring the frequency and duration of periods of apneas and hypopneas during a full night and subsequent interpretation of collected data generates the apnea-hypopnea-index (AHI), also known as the number of pharyngeal collapses per hour during sleep. In some clinics, this requires admission to the hospital and specific equipment and hence is time consuming and costly.

Increasing the pressure in the upper airway to prevent its collapse is the essence of managing OSA. The employment of continuous positive airway pressure (CPAP) devices has significantly reduced OSA associated mortality rates in large cohorts of individuals[6].

OSA is an important risk for perioperative complications in morbidly obese patients undergoing surgeries requiring general anesthesia[4]. We report our experience with routine clinical and ambulatory PSG and ambulant polygraphy (PG) in a cohort of patients undergoing bariatric surgery to assess the true prevalence of OSA with respect to the different severity levels as determined by the AHI and to evaluate whether this protocol is necessary to increase perioperative safety.

MATERIAL AND METHODS

Study design and population

All patients who underwent bariatric surgery met the International Federation for the Surgery of Obesity and Metabolic Disorders criteria for bariatric surgery and were consecutively entered in a database. From 2012 onwards, the performance of P(S)G prior to bariatric surgery became mandatory. Therefore, all bariatric surgery patients were considered eligible since 2012. Patients who underwent either a laparoscopic Roux-en-Y gastric bypass (LRYGB) or laparoscopic sleeve gastrectomy (LSG) were included. Both primary and revisional procedures were included. P(S)G and bariatric surgical procedures were performed as previously described[3;10].

Data on AHI were retrospectively collected from patient medical records and registered in an anonymous database. According to the international guidelines, OSA is diagnosed when the AHI is ≥ 5/hour; moderate OSA is defined as an AHI ≥ 15/hour, severe OSA is present when AHI ≥ 30/hour. The prevalences of AHI ≥ 60/hour and ≥ 90/hour were also given in order to illustrate the severity and risk of some bariatric surgery patients.

Patients were referred to a pulmonologist for CPAP therapy when indicated. Indications were mostly an AHI ≥ 15/hour, severe clinical symptoms or high AHIs in supine position. CPAP was prescribed in the preoperative period and patients were asked to bring their CPAP mask and machine during admission. Prior to surgery, all patients were evaluated by an anesthesiologist, who decided whether patients required postoperative Intensive Care Unit (ICU) admission. In most cases, this was decided when the AHI was greater than 30/hour.

The Institutional Review Board provided approval for this study. Informed consent was not necessary for this retrospective study design.

Statistical analysis

The number of patients with an AHI ≥ 5/hour, 15/hour, 30/hour, 60/hour and 90/hour was calculated. The number of patients that should undergo preoperative sleep registration to detect these AHIs was calculated with the following formula: 100 / (% of patients with an AHI ≥ 5/hour, 15/hour, 30/hour, 60/hour or 90/hour) and expressed as round number (i.e. 3.4 is rounded up to four). As the revisional surgery group is known to have lower preoperative BMIs, and therefore lower AHIs, the analyses were performed for the total study population, the primary surgery group and the revisional surgery group. Secondly, the number of CV, pulmonary and neurovascular complications were registered and compared between OSA severity groups, according to international definitions i.e. AHI 0-5/hour, 5-15/hour, 15-30/hour and ≥30/hour.

RESULTS

Study population

From January 2012 until October 2015, a total of 1417 patients underwent a LRYGB or LSG. The preoperative AHI was missing in 59 patients due to several reasons (operation in 2012 (n=30), P(S)G (and treatment) elsewhere (n=26) or other reasons (n=3). Consequently, the AHI was available in 1358 (95.8%) patients who were therefore included.

Primary surgery was performed in 1154 (85%) patients, of which 1069 (78.7%) patients underwent a primary LRYGB and 85 (6.3%) a primary LSG. Consequently, 204 (15%) patients underwent revisional surgery, mostly from Laparoscopic Adjustable Gastric Banding (LAGB) in to LRYGB (n=183; 89.7%). Other procedures were LAGB to LSG (n=10; 0.7%), LSG to LRYGB (n=8; 0.6%) or LRYGB revisions such as pouch revision (n=3; 0.2%). The study population consisted of 1126 (82.9%) women and 232 (17.1%) men. The mean age was 44.4 years (SD 10.8); mean BMI was 44.1 kg/m^2 (SD 6.4). The median AHI of the entire study population was 7.0/hour (interquartile range 16.4).

Prevalence OSA

The numbers of patients with an AHI ≥ 5/hour, ≥ 15/hour, ≥ 30/hour, ≥ 60/hour or ≥ 90/hour are displayed in **Table 1**. The number of bariatric surgery patients that should undergo sleep registration to detect these AHI severity levels are shown in **Table 2**.

A total of 410 patients (30.2%) received CPAP therapy (n=406) or Mandibular Repositioning Appliance (n=4) and 280 patients (20.6%) were admitted to the ICU during the first night after surgery.

Table 1 - Number of patients with AHI ≥ 5, 15, 30, 60 and 90

Variable	Total study group (n=1358)	Primary surgery group (n=1154)	Revisional surgery group (n=204)
AHI ≥ 5/hour; n (%)	813 (59.9)	711 (61.6)	102 (50)
AHI ≥ 15/hour; n (%)	405 (29.8)	365 (31.6)	40 (19.6)
AHI ≥ 30/hour; n (%)	213 (15.7)	193 (16.7)	20 (9.8)
AHI ≥ 60/hour; n (%)	79 (5.8)	71 (6.2)	8 (3.9)
AHI ≥ 90/hour; n (%)	17 (1.3)	15 (1.3)	2 (1)

AHI = Apnea-Hypopnea-Index

Table 2 - Number of bariatric patients that should undergo P(S)G to detect an AHI ≥ 5, 15, 30, 60 and 90

Variable	Total study group (n=1358)	Primary surgery group (n=1154)	Revisional surgery group (n=204)
AHI ≥ 5/hour	2	2	2
AHI ≥ 15/hour	4	4	6
AHI ≥ 30/hour	7	6	11
AHI ≥ 60/hour	18	17	26
AHI ≥ 90/hour	77	77	100

AHI = Apnea-Hypopnea-Index
P(S)G = Poly(somno)graphy

Postoperative complications

CV, pulmonary and neurovascular complications occurred in 31 patients (2.3%) in the 30-day postoperative period. Out of these 31 patients, 16 were in combination with a surgical complication i.e. anastomotic leakage, bleeding, stenosis or perforation. AHI class had no effect on this occurrence (Table 3).

Death occurred in four patients (0.3%) due to surgical causes: asystole due to abdominal sepsis after anastomotic leakage (n=1; AHI 50/hour), subarachnoid hemorrhage after persistent anastomotic leakage (n=1; AHI 8.1/hour); ventricular fibrillation after anastomotic leakage (n=1; AHI 23.5/hour); cardiac tamponade due to iatrogenic injury during surgery (n=1; AHI 23/hour). There was no OSA related mortality.

Table 3 - Cardiovascular, pulmonary and neurological complications in the 30 day postoperative period

	Complication within 30 days	
Variable	No (n=1327)	Yes (n=31)
AHI 0-5/hour; (%)	534 (40.2)	11 (35.5)
AHI 5-15/hour; (%)	401 (30.2)	7 (22.6)
AHI 15-30/hour; (%)	185 (13.9)	7 (22.6)
AHI ≥ 30/hour; (%)	207 (15.6)	6 (19.4)

AHI = Apnea-Hypopnea-Index; p=0.452

DISCUSSION

OSA is a potentially life-threatening condition when not detected and managed appropriately. In current cohort, all patients underwent mandatory OSA screening prior to surgery. Although postoperative cardiovascular, neurovascular and pulmonary complications were found in current cohort, no significant difference was detected between OSA severity groups. As OSA has shown to be a significant risk factor for postoperative cardiac events and respiratory failure in literature[7-8], this suggests that early recognition and adequate treatment is successful in decreasing OSA related complications.

The best available method to identify the severity of OSA is PSG. However, routine PSG measurements in obese patients undergoing bariatric surgery have not been accepted as standard modality. In our study of 1358 patients undergoing bariatric surgery, one-third of all patients had more than 15 apneas and hypopneas per hour when measured during P(S)G. These numbers are probably even higher as many patients underwent a PG instead of a PSG. A PG records the same parameters as a PSG except for the sleep architecture. Therefore, a PG measures the average AHI during a full night without differentiating between sleep and wake periods, whereas a PSG measures the average AHI only during sleep periods. As the AHI is zero when awake, patients who underwent a PG instead of a PSG might have an underreported AHI[10]. Although PG is less time consuming than PSG, mild OSA might be missed. However, the clinically more relevant moderate and severe OSA will still be detected. PG is therefore recommended as a less expensive but valuable alternative to PSG. Screening questionnaires should however be avoided as these have failed to diagnose OSA accurately[3;9]. Although some questionnaires such as the STOP-BANG questionnaire can detect OSA patients, no questionnaire gives a sensitivity of 100%. Additionally, we often see patients in our clinic without clinical symptoms who appear to have severe OSA during P(S)G. Unfortunately we are not able to present these numbers as clinical symptoms were not documented consequently.

Discussion persists about the correlation between severity of OSA and perioperative risk in specific bariatric surgery patients[11]. In centers considering an AHI greater than 30 as a considerable risk, one out of seven sleep studies would detect one high risk patient. Other centers adhering to a threshold of an AHI greater than 60, 18 sleep studies would yield one high risk patient, while at a threshold of more than 90, 77 sleep studies would be required. In patients with very high AHI levels and poor CPAP compliance, admission to a clinical unit with continuous monitoring is recommended[4].

The number needed to screen is formally the number of patients that should be screened to prevent morbidity or mortality. Unfortunately, it is not possible to accurately determine the relationship between OSA and morbidity and mortality after bariatric surgery, as the presence of OSA has been poorly assessed in available bar-

iatric studies[11]. Therefore, we used the AHI as parameter for determining the number needed to screen.

In conclusion, OSA is present in the majority of bariatric surgery patients. Moreover, one-third of the bariatric surgery patients have an AHI greater than 15/hour and would benefit of CPAP therapy. In current study, no effect of OSA severity was seen on CV, pulmonary and neurovascular outcomes, possibly due to early recognition and adequate treatment of OSA. In order to increase perioperative safety and avoid the preventable risk of perioperative complications, we recommend mandatory P(S)G prior to bariatric surgery.

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Biomarkers for diagnosing obstructive sleep apnea in bariatric patients

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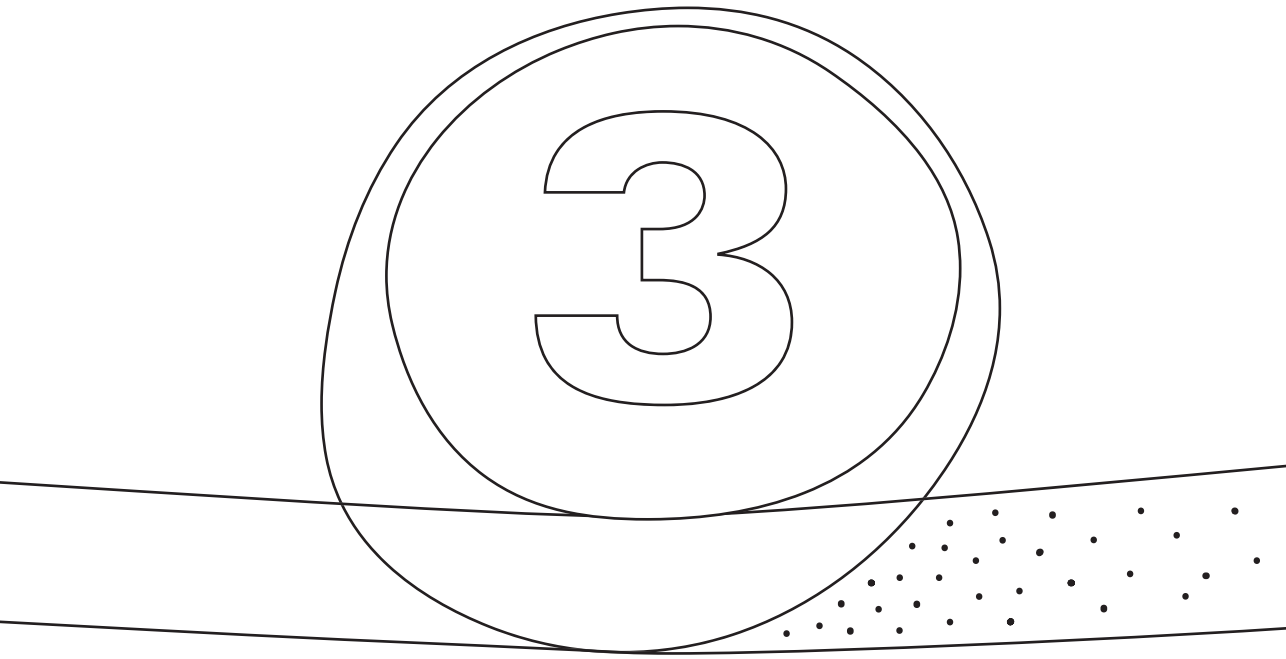

ABSTRACT

Introduction: Obstructive sleep apnea (OSA) is a common comorbidity in bariatric patients and should be recognized in the perioperative setting to reduce the risk of adverse events. Polysomnography (PSG) is considered the gold standard for OSA diagnosis, but is time consuming, expensive and often impossible to perform on routine basis in high volume bariatric centers.

Objectives: To identify biomarkers associated with OSA and assess the validity of a biomarker prediction model as a screening tool for (moderate and severe) OSA in bariatric surgery.

Methods: In this prospective cohort study all patients scheduled for primary laparoscopic Roux-en-Y gastric bypass and laparoscopic sleeve gastrectomy were considered eligible for inclusion. Clinical data, PSG and plasma were collected from every patient prior to surgery. Three out of 27 biomarkers were selected for a prediction model for OSA. According to sample size calculation, 90 patients were required for the training set and 45 for the validation set.

Results: After excluding nine patients, a final 126 patients were included for further analyses. OSA was diagnosed in 73 (57.9%) patients. The optimal prediction model for OSA included plasminogen activator inhibitor-1, angiopoietin-like protein 7 and Tumor necrosis factor-alpha. The area under the curve (AUC) for apnea-hypopnea-index (AHI) ≥ 5/hour was 0.77 (95% C.I. 0.635-0.908) and AHI ≥ 15/hour 0.81 (95% C.I. 0.660-0.941). Sensitivity and specificity were 95% and 63% respectively for the optimal cutoff value of biomarker-AHI ≥ 7/hour for PSG-AHI ≥ 15/hour.

Conclusion: Current prediction model has a fair AUC, but wide confidence interval, caused by a small study population. In its current form, the model cannot replace the P(S)G, but can be used to rule out moderate or severe OSA in 23% of patients and withhold them from preoperative P(S)G.

INTRODUCTION

Obstructive sleep apnea (OSA) is a sleep breathing disorder associated with hypoxemia and hypercapnia. Non-specific signs such as snoring, daytime sleepiness, obesity and hypertension are often thought to be related to other problems than OSA. Especially in the morbidly obese population of whom most (> 60 %[1]) are affected by OSA, complaints are easily contributed to their obesity. The complex pathophysiology of OSA cause unrecognized OSA to increase the risk of multi organ morbidity in the long-term[2]. Surgeries requiring general anesthesia are known to increase OSA related perioperative risks[3]. Considering these arguments, one could understand consensus guidelines to recommend routine OSA screening in the preoperative management of morbidly obese patients scheduled for bariatric surgery.

Recognition of OSA and its risks in the bariatric population has improved over the last few years. Performing mandatory sleep studies in all bariatric patients, however, remains a challenging task. Over 600,000 bariatric procedures are performed worldwide on annual basis and this number is still rising[4]. Sleep centers often lack capacity to perform sleep studies for such large patient groups; there is a short period of time prior to surgery when a sleep study can be performed; sleep studies are considered burdensome to the patient; and they are costly. The gold standard to diagnose OSA is polysomnography (PSG)[1]. Polygraphy (PG) has shown to be a good alternative in this high risk group, but screening questionnaires that have been developed as a quick and free of costs method to screen for OSA are not accurate enough to replace sleep studies in the bariatric population[1].

Biomarkers collected from venipuncture are less expensive, less time consuming and more patient friendly than PSG. Replacement of PSG for accurate biomarkers would provide an opportunity for all bariatric clinics to perform standard OSA screening prior to bariatric surgery and during follow-up.

This study aimed to identify biomarkers associated with OSA in bariatric surgery patients by investigating whether there are biomarkers in agreement with PSG in the preoperative period.

METHODS

Study design and population

Patients were recruited in the OLVG hospital in Amsterdam, the Netherlands. All patients scheduled for primary laparoscopic Roux-en-Y gastric bypass (LRYGB) or laparoscopic sleeve gastrectomy (LSG) were eligible for inclusion in this prospective cohort study. Those undergoing other bariatric surgical procedures such as revisional surgery were excluded from this cohort. The study was approved by the medical ethical committee and all included patients gave written informed consent.

Data collection

Included patients were anonymously entered in a consecutive database. Baseline characteristics including PG/PSG outcomes were collected from medical records. In the OLVG, it is common practice that all bariatric patients undergo preoperative PG/PSG on routine basis. OSA is defined as an apnea-hypopnea-index ≥ 5/hour and can be divided in mild (AHI 5-15/hour), moderate (AHI 15-30/hour) and severe (AHI ≥ 30/hour) OSA. Those with moderate or severe OSA are referred to the pulmonologist for treatment with continuous positive airway pressure (CPAP). An additional procedure for this specific study was plasma collection from venipuncture. Ten ml of blood was collected using vacutainer tubes and then aliquoted and stored at -80°C. The samples were then packed in dry ice and send to the Dasman Diabetes Institute (DDI) in Kuwait City, Kuwait for further assays. Samples were analyzed using bioplex software-Luminex 200 biorad platform, Gen5 software-Synergy H4 platform.

Surgical procedures

The LRYGB and LSG are the two most performed bariatric procedures worldwide. Both are performed laparoscopically and according to standardized techniques[5]. Reducing the size of the stomach is a key component of the LRYGB as well as the LSG. In a LRYGB, an additional proximal intestinal bypass is performed to increase malabsorption.

Biomarkers

A biomarker is a measurable indicator of some biological state or condition. OSA is known for its complex multifactorial pathophysiology and is associated with changes in glucose metabolism, lipid metabolism, levels of growth factors, inflammation and sleep wakefulness[6]. Combining obesity related factors have been used previously to predict OSA, for example in screening questionnaires[7]. In this study we aimed to evaluate the predictive value of each independent biomarker and hence analyze whether a combination of the strongest biomarkers could create a clinically valuable prediction model. Included biomarkers and their explanation are displayed in **Appendix 1**.

Sample size calculation

The current prevalence of OSA (AHI>5) in bariatric patients is 70%. If no test or assay was performed and all bariatric patients were treated as if they had OSA – 30% of bariatric patients would be treated unnecessarily. It was aimed to find a biomarker that will decrease this proportion (false positive rate (1-specificy)) to 10% - meaning a specificity of 90%, and to minimize the risk of not correctly diagnosing patients with OSA to 80% - assuming a test sensitivity of 80%.

The training set will be used to initially select an optimally predictive set of at most three out of 27 biomarkers. Using the standard rule of a minimum of 10 events (here being patients) per predictor in the smallest outcome category (here being the bariatric patients without OSA making up 30% of all bariatric patients) – enrolling 90 patients (approximately 27 patients without OSA; 63 with OSA) would be sufficient to reliably estimate multivariate logistic regression models with a maximum of three biomarkers. The final model will subsequently be validated on 45 additional patients. The area under the curve (AUC) for the best performing linear predictor selected using the training set will be calculated. Including 45 patients (13 without OSA) would give an 80% power to reject the null-hypothesis that the AUC = 0.5 under the alternative that the AUC is 0.8 (the minimal required sensitivity of 80% and specificity of 90% correspond to an AUC of approximately 0.85).

Statistical analyses

All data were analyzed using SPSS 21.0 for Windows (SPSS Inc. Chicago Illinois, USA) and StataSE 14 for Windows (StataCorp LLC., Texas, USA). Continuous baseline variables were compared between OSA and non-OSA patients with independent t-test or Mann-Whitney U test, depending on normality evaluated with histograms. Categorical variables were compared with Chi-square test.

Univariable regression analyses of all biomarkers were performed in the training set. Biomarkers associated with OSA ($p < 0.10$) were selected for multivariable analyses. Prior to these analyses, linearity was checked between continuous biomarkers and outcomes. Those showing non-linearity were divided into quartiles creating ordinal variables. The best performing biomarkers in multivariable logistic regression were identified using forward selection ($p < 0.05$); these predictors remained in the final model. Explained variance was calculated with adjusted R-square to derive the quality of the model. The study is reported in accordance with the TRIPOD guidance for transparent reporting of prediction models.

Agreements between P(S)G-AHI and Biomarker-AHI were calculated with intra-class correlation coefficient (ICC) ± 95% confidence intervals (CI) by using two-way mixed effects model for single measurement (Bland & Altman plots). The ICC varies between zero (no agreement) and one (perfect agreement) and can be categorized in poor (ICC < 0.5), moderate (ICC 0.5-0.75), good (ICC 0.75-0.9) and excellent (ICC > 0.9). Mean difference and 95% limits of agreement were provided to represent the average difference (bias) between both outcomes and variation of P(S)G-AHI and Biomarker-AHI respectively. In the validation set, the area under the curve (AUC) and cut-off values for the highest sensitivity and specificity were calculated.

RESULTS

Of the 135 included patients, nine patients were excluded for further analyses. Eight dropped out due to missing venipuncture material and one appeared to have undergone revisional surgery from LSG to LRYGB.

Out of 126 patients, 110 (87.3%) are female and 16 (12.7%) male. OSA (AHI ≥ 5/hour) was diagnosed in 73 (57.9%) patients. Mean age was 44.9 (SD 12.8) years; mean BMI was 43 (SD 6.7) kg/m^2.

Primary LRYGB was performed in 107 (84.9%) patients, primary LSG in 17 (13.5%) patients. Two (1.6%) patients cancelled the operation. PSG and PG were performed in 115 (91.3%) and 11 (8.7%) patients respectively. CPAP was used in 45/73 (58.9%) OSA patients. OSA patients are more frequently male, older and have a higher BMI. Baseline characteristics are displayed in Table 1.

Table 1 - Baseline characteristics total study population (n=126)

Variables	non-OSA (n=53)	OSA (n=73)	p-value
Female (%)	50 (94.3)	60 (82.1)	0.040
Male (%)	3 (5.7)	13 (17.8)	
Age (SD)	41.7 (11.9)	48.6 (12.2)	0.002
BMI (SD)	41.5 (4.8)	43.8 (7.2)	0.000
AHI (IQR)	2.4 (1.5)	21.5 (16.2)	0.000
AI (IQR)	0.4 (0.6)	6.8 (9.6)	0.000
HI (IQR)	1.9 (1.4)	14 (10.4)	0.000
% TST in supine position (IQR)	30.7 (27)	38.3 (28)	0.132
AHI in supine position (IQR)	6.2 (12.5)	25.7 (20.2)	0.000
Cholesterol (SD)	5 (0.9)	5.3 (1)	0.158
Triglyceride (IQR)	1.9 (2)	2.2 (1.1)	0.231
HDL cholesterol (SD)	1.3 (0.3)	1.2 (0.3)	0.464
LDL cholesterol (SD)	3.2 (0.9)	3.4 (0.9)	0.173

AHI = Apnea Hypopnea Index; BMI = Body Mass Index; IQT = Interquartile Range; OSA = Obstructive Sleep Apnea; SD = Standard Deviation; TST = Total Sleeping Time

Univariable regression analyses

Biomarkers that were associated with the AHI ($p < 0.10$) were selected for multivariable analyses. Results of 27 biomarkers are shown in Table 2.

Prediction model

The best prediction model in the test group (n=81) includes plasminogen activator inhibitor-1, angiopoietin-like protein 7 and Tumor necrosis factor-alpha (Table 3). The explained variance was 0.178, meaning that over 82% of OSA is explained by other factors.

Table 2 - Univariable regression analyses biomarkers

	β-regression coefficient (n=81)	p-value (n=81)
1. Cpep	.0007385	0.478
2. Ghrelin	-.0023009	0.268
3. GIP	-.0002672	0.858
4. GLP1	-.0081873	0.441
5. Glucagon	.004261	0.927
6. Insulin	.002204	0.116
7. Leptin	-.0000856	0.472
8. PAI1	.0016954	0.002*
9. Vesfatin	-.0001274	0.336
10. ANGPTL3	.0001088	0.064
11. CCL11	.051009	0.197
12. IGFBP3	9.50e-06	0.274
13. LeptinR	.0000741	0.559
14. TNFα	.9736736	0.057*
15. ANGPTL4	-.0000347	0.122
16. FGFa	.0092299	0.489
17. IGFBP4	.0131518	0.291
18. ANGPTL6	-.0000462	0.530
19. IGFBP1	.0001395	0.065*
20. IL6	2.272886	0.052*
21. Resistin	-.000161	0.641
22. DNAJC27	.9440743	0.151
23. FactorD	.0035143	0.072*
24. ANGPTL7	.0004122	0.012*
25. ANGPTL8	.0095968	0.002*
26. DNAJB3	4.266422	0.032*
27. Orexin	-.0000826	0.992

* Included in multivariable linear regression analysis ($p < 0.10$).

Table 3 - Prediction model

	β-regression coefficient (n=81)	95% confidence interval	p-value (n=81)
PAI1	0.0014914	0.0002531-0.0027297	0.01
TNFα	0.9160808	-1.789143-3.621304	0.05
ANGPTL7	0.0003599	0.0000999-0.0006199	0.02
Constante	-13.05027		

The explained variance was: Adjusted R-square: 0.177 (18% of the variance in AHI can be explained by the biomarker prediction model)

Prediction values by the prediction model and the P(S)G-AHI showed poor agreement (ICC 0.42, 95% CI 0.14-0.63). The Bland-Altman plot showed a mean difference of 0.80 between the Biomarker-AHI and the P(S)G-AHI, meaning that the Biomarker-AHI values were on average 0.80 lower than the P(S)G-AHI values. The limits of agreement estimated an interval of –24.1 to 25.71, which indicates that the biomarker model may measure as much as 24.1 below and 25.71 above the P(S)G values (Figure 1).

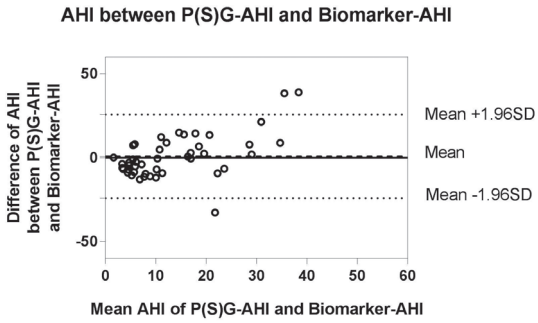

Figure 1 - Bland-Altman plot of P(S)G-AHI and Biomarker-AHI
Each circle represents a value measured by P(S)G-AHI and Biomarker-AHI. Mean difference 0.80, limits of agreement -24.1 to 25.71).

Diagnostic accuracy

The AUC for AHI ≥ 5/hour is 0.77 (95% C.I. 0.635-0.908) and for AHI ≥ 15/hour 0.81 (95% C.I. 0.660-0.941). The receiver operating characteristic curve for the latter is shown in Figure 2.

Validity measures of different cutoff measures of the biomarker model were compared with simultaneous P(S)G (cutoff value AHI ≥ 15/hour). For exclusive diagnosis (screening) the sensitivity for the optimal cutoff value of biomarker-AHI ≥ 7/hour was 95%. In this study, 23% had a biomarker-AHI < 7/hour. This means that current model reliably excludes moderate and severe OSA in 23% of bariatric patients, saving them further P(S)G. For definitive diagnosis, specificity for biomarker-AHI ≥ 7/hour was 63%.

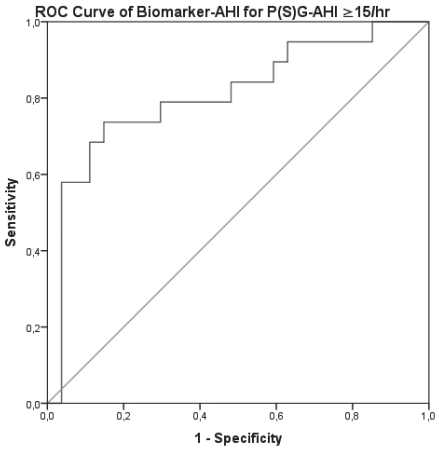

Figure 2 - Receiver operating characteristic curve of Biomarker-AHI for P(S)G-AHI ≥15/hour. Area under the curve: 0.81; 95% confidence interval: 0.67-0.95; $p < .01$.

DISCUSSION

OSA is a common comorbidity in morbidly obese subjects and should be recognized in the perioperative setting to reduce the risk of adverse events. In bariatric surgery, stratifying this risk is rather important than defining the exact AHI as AHI reduction following weight loss is expected postoperatively. This allows clinicians to use a simple screening tool for OSA instead of an expensive and time consuming sleep study in the bariatric population.

Evaluation of 27 biomarkers collected from venipuncture resulted in a prediction model of three markers. External validation analyses (n=45) showed an AUC of 0.77 (AHI ≥ 5/hour; 95% C.I. 0.635-0.908) and 0.81 (AHI ≥ 15/hour; 95% C.I. 0.660-0.941), indicating a fair screening tool. Wide confidence intervals, however, make the model not applicable in its current form. Valuable prediction models in the clinical setting should include small intervals. Future studies should focus on decreasing the 95% confidence interval by increasing the data set. Larger sample sizes are additionally valuable for internal validation of prediction models by bootstrap techniques and indicative for the model's performance in future patients. Imputation techniques to handle missing data were not required in this study due to the low percentage of missing data.

Our goal was to provide a screening tool including categorical variables with cut-offs rather than finding a model with continuous biomarker values. The latter, however, gives insight in the complex multifactorial pathophysiology of OSA. Explained variance of the exact AHI when using continuous biomarker values was only 18%, meaning 82% of AHI is explained by other factors. Many OSA associated factors are described in literature. Examples are older age, male gender, high BMI, high neck- and waist circumference, hypertension and type II diabetes. Increasing severity of the continuous characteristics increases the AHI, but none reliably predicts OSA severity. This suggests that the AHI is influenced by other factors as well.

A challenging issue is the fact that current biomarkers are influenced by multiple factors, and the same markers have multiple influences too. They are not only correlated with OSA, but also with type II diabetes, inflammation, lipid metabolism, etcetera. This makes OSA diagnosing very complex.

Another option to tackle the problem with AHI is using a different OSA severity metric for example the oxygen desaturation index (ODI). In a recent study with a simple sleep monitor called the "Check me pro", the ODI appeared to be a reliable metric to exclude moderate and severe OSA in bariatric patients[8]. With a sensitivity and negative predictive value of 100% and 100%, this monitor enables bariatric clinics not to perform PSG in all patients scheduled for surgery. Using this sleep monitor is less time consuming, more patient friendly and less expensive than P(S)G. A prediction model of biomarkers collected from venipuncture would be superior regarding all these aspects and hence a challenging next step. Comparison of pre- and

postoperative data could give more insight in the changes of biomarker values and AHI and hence could change the composition of biomarkers in a prediction model.

In conclusion, current prediction model has a fair AUC, but wide CI caused by a small study population. In its current form, the model cannot replace the P(S)G, but can be used to rule out moderate or severe OSA in 23% of patients and withhold them from preoperative P(S)G.

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Appendix 1 - Biomarkers

- C-peptide is a widely used measure of pancreatic beta cell function and can assess a person's own insulin secretion.
- Ghrelin and leptin/Leptin R (leptin receptor) play an important role in regulating appetite and in the distribution and rate of energy use.
- GIP (Gastric inhibitory polypeptide) and GLP-1 (Glucagon-like peptide 1) are hormones that belong to a family of incretins that play a role in regulating insulin secretion.
- Glucagon and insulin are peptide hormones that play an active role in allowing the body to regulate the utilization of glucose and fats.
- PAI-1 (Plasminogen activator inhibitor-1), resistin, vesfatin and CCL11 are chemokines that were found to play a role in obesity and type II diabetes.
- ANGPTL 3, 4, 6, 7and 8 are Angiopoietin-like proteins that play a role in lipid metabolism.
- IGFBP 1,3 and 4 Insulin-like growth factor-binding proteins are the principal regulators of IGF-1 and IGF-2 action. Accordingly, effects of IGFBPs can be observed on the levels of growth and differentiation, development, metabolism, and lifespan.
- DNAJB3 and DNAJC27 are heat shock proteins belonging to the HSP40 family. They play a role in obesity and type II diabetes.
- FGF (Fibroblast Growth Factors) are a family of growth factors which play an important role in tissue repair and regeneration.
- Factor D (adipsin) is an adipokine that improves β cell function in diabetes.
- TNF-α (Tumor necrosis factor-alpha) and IL-6 are cytokines involved in systemic inflammation.
- Orexin is a Neuropeptide that plays a significant role in the regulation of food intake and sleep-wakefulness.

Appendix 2 - Univariate analyses plasma training set (n=81)

Variables	non-OSA (n=53)	OSA (n=73)	p-value
C-peptide; pg/ml (IQR)	2872.85 (3614.99)	2919.52 (2712.17)	0.445
Ghrelin; pg/ml (IQR)	2505.63 (1228.43)	2130.58 (1075.62)	0.128
GIP; pg/ml (IQR)	2043.92 (1850.51)	1437.91 (1246.38)	0.156
GLP-1; pg/ml (IQR)	358.1 (133.95)	335.76 (120.79)	0.182
Glucagon; pg/ml (IQR)	2545.53 (375.61)	2584.37 (324.99)	0.366
Insulin; pg/ml (IQR)	1328.71 (2012.11)	1563.37 (1544.71)	0.818
Leptin; ng/ml (IQR)	27786.52 (14616.82)	25154.1 (16965.90)	0.884
PAI-1; ng/ml (IQR)	11202.55 (3963.77)	11185.78 (5078.59)	0.448
Vesfatin; ng/ml (IQR)	21328.5 (6735.1)	20244.73 (8729.02)	0.232
ANGPTL3; ng/ml (IQR)	57205.79 (31368.96)	58783.62 (33263.51)	**0.010**
CCL11; pg/ml (IQR)	28.73 (40.29)	39.09 (48.65)	0.459
IFGBP-3; ng/ml (IQR)	618070.07 (249120.14)	622023.57 (259188.76)	0.445
Leptin R; ng/ml (IQR)	22490.48 (16948.36)	27688.65 (17945.74)	0.221
TNF-alpha; pg/ml (IQR)	1.16 (2.37)	1.94 (2.72)	0.112
ANGPTL4; ng/ml (IQR)	166974.57 (141116.53)	140653.05 (63954.69)	0.173
FGF acidic; pg/ml (IQR)	11.9 (5.71)	11.9 (7.66)	**0.021**
IGFBP-4; pg/ml (IQR)	131.03 (156.26)	183.25 (275.73)	0.402
ANGPTL6; pg/ml (IQR)	31101.04 (19073.72)	34166.9600 (20027.55)	0.267
IGFBP-1; pg/ml (IQR)	2507.66 (3334.82)	2955.19 (7087.05)	0.302
IL-6; pg/ml (IQR)	2.24 (1.36)	2.37 (1.9)	0.615
Resistin; ng/ml (IQR)	11796.41 (5144.95)	10605.63 (7673.14)	0.207
DNAJC27; ng/ml (IQR)	1.64 (4.02)	2.41 (2.95)	0.515
Factor D; ng/ml (IQR)	3612.18 (846.84)	4054.33 (1288.99)	**0.011**
ANGPTL7; ng/ml (IQR)	17216.54 (15016.60)	21126.08 (18567.77)	0.243
ANGPTL8; pg/ml (IQR)	680 (615.39)	878.6700 (1150.77)	0.064
DNAJB3; ng/ml (IQR)	0.75 (0.52)	0.94 (1.19)	0.111
Orexin; ng/ml (IQR)	127.29 (60.58)	113.27 (43.44)	0.259

Validity of a simple sleep monitor for diagnosing obstructive sleep apnea in bariatric surgery patients

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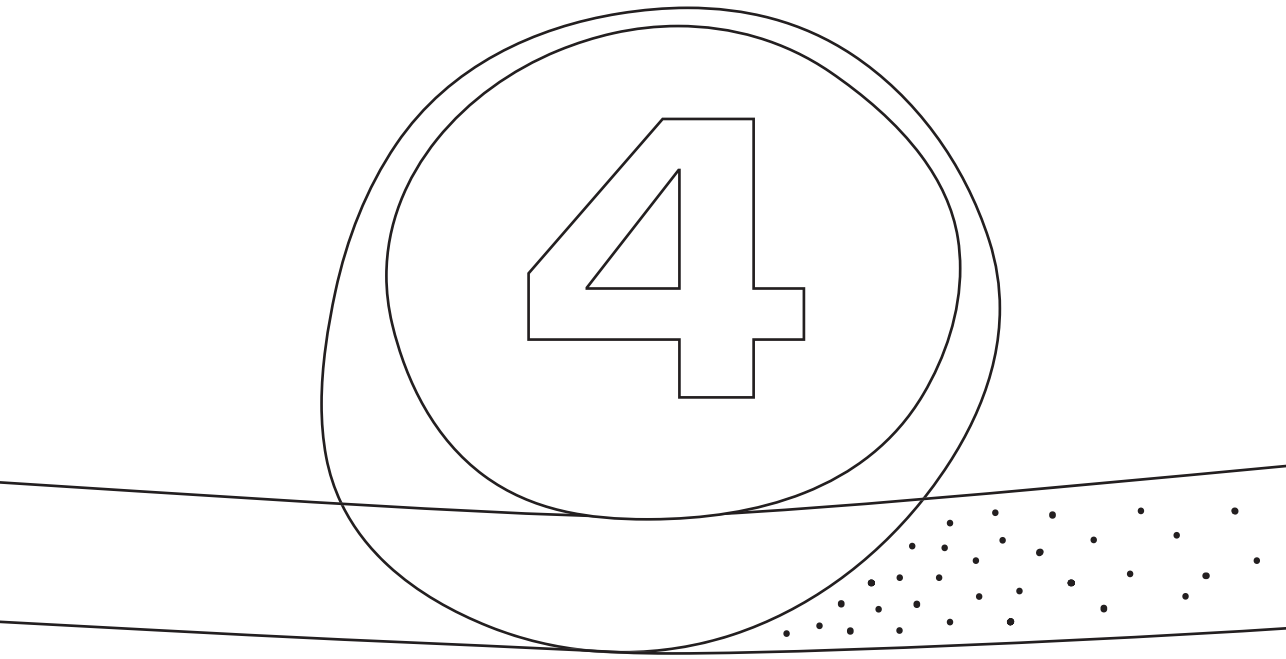
Surg Obes Relat Dis 2018 Jul;14(7):1020-1025



ABSTRACT

Introduction: One-third of bariatric surgery patients have an apnea-hypopnea-index (AHI) greater than 15/hour, representing moderate and severe forms of obstructive sleep apnea (OSA). Treating these forms of OSA is recommended to reduce the risk of perioperative complications. The AHI derived from polysomnography (PSG) is the gold standard for OSA diagnosis. However, performing PSG in all patients scheduled for bariatric surgery is time consuming and expensive. An accurate and simple screening tool able to rule out moderately to severe OSA would reduce the number of patients needing mandatory PSGs.

Objectives: To assess the validity of a simple sleep monitor (Checkme Health Monitor (BodiMetrics/Viatom Technology)) as a screening tool for OSA in bariatric surgery patients.

Setting: Obesity Center Amsterdam, OLVG-west, Amsterdam, the Netherlands

Methods: Patients scheduled for bariatric surgery were prospectively enrolled in this study. All patients underwent pre-operative P(S)G and simultaneously used the Checkme to assess the oxygen desaturation index (ODI). The diagnostic performance of the Checkme for AHI ≥15/hour was assessed using Receiver Operating Characteristic (ROC) curve analysis.

Results: A total of 50 patients were analyzed. Sensitivity and negative predictive value (NPV) were 100% and 100% respectively, specificity and positive predictive value (PPV) were 69% and 64% respectively for the optimal cutoff value of Checkme-3%ODI ≥ 9/hour for P(S)G AHI ≥ 15/hour. The area under the curve (AUC) value expressed by the ROC curve was 0.95.

Conclusion: The Checkme is valid for exclusion of moderate and severe OSA in bariatric surgery patients. The Checkme enables bariatric clinics not to perform PSG in all patients scheduled for bariatric surgery.

INTRODUCTION

Obstructive sleep apnea (OSA) is a common comorbidity in severe and complex obesity, reaching a prevalence of 60-70% in bariatric surgery patients who present for preoperative evaluation[1,2]. Patients with OSA have an increased risk for perioperative and postoperative complications following bariatric surgery when not detected and managed appropriately[3]. Treatment of OSA is generally indicated for moderate-to-severe forms, defined as an apnea–hypopnea index (AHI) score of ≥ 15 per hour[4].

The AHI derived from polysomnography (PSG) is the gold standard for OSA diagnosis. Evaluation of OSA in the preoperative setting is time consuming and labor intensive. Moreover, performing mandatory PSG goes along with high costs and logistic difficulties in high volume bariatric centers. Such disadvantages urge to look for alternative reliable screening tools that could be used in routine clinical practice for identification of OSA in bariatric surgery patients. An accurate and simple screening tool able to rule out moderate and severe OSA would reduce the number of patients needing mandatory PSGs.

Numerous screening tests have been developed to identify patients with a high-risk of OSA[5]. In bariatric surgery, however, a limited number of screening tests have been validated for preoperative evaluation of OSA. As bariatric surgery patients differ from the general population in many baseline characteristics, screening test should be validated for this specific population. The available screening questionnaires, clinical prediction tools and devices for OSA have never reached a sensitivity of 100% in the bariatric surgery population with the consequence that patients with OSA are not referred for further evaluation and appropriate treatment[1,5-10]. Furthermore, many available screening tests have a very high proportion of positive results in the bariatric population through which only a few patients could be saved from further testing.

The Checkme is a new device that has recently become available. The Checkme is a small and handheld device that measures the oxygen desaturation index (ODI) with a pulse oximeter during sleep. OSA is characterized by repeated episodes of upper airway collapse that are responsible for desaturations. This suggests that not only the AHI but also the ODI could indicate presence of OSA. An accurate screening tool identifying patients at risk of OSA would provide an opportunity for all bariatric clinics to perform standard OSA screening prior to bariatric surgery and during follow-up.

The purpose of the study is to validate the Checkme as a screening tool for OSA in bariatric surgery patients by comparing the results with the reference standard PSG.

METHODS

Study design and population

We performed a prospective, single-center pilot study involving patients scheduled for primary or revisional bariatric surgery in the OLVG West, Amsterdam, The Netherlands. Bariatric surgery patients were included consecutively. All patients met the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) criteria for bariatric surgery[11]. In the OLVG West, Amsterdam, ambulant polygraphy (PG) and, in some cases, ambulant PSG is routine preoperative care in bariatric surgery patients. As the performance of P(S)G prior to bariatric surgery is mandatory in the OLVG West, all patients were considered eligible for inclusion. Only patients who did not undergo P(S)G due to previous diagnosis of OSA were excluded from the study. Patients underwent pre-operative P(S)G and were asked to simultaneously use the Checkme at home for one night. The local Institutional Review Board provided approval for this study, and patients provided informed consent prior to participation in the study.

Poly(somno)graphy

The P(S)G was performed as previously described using Somnoscreen (Somnomedics BV) portable recording device[2, 12]. The number of apneas and hypopneas per hour of sleep (AHI) generated by the P(S)G was used to indicate OSA severity. OSA was defined as an AHI greater than 5/hour and was further categorized in mild OSA (AHI 5-15/hour), moderate OSA (AHI 15-30/hour) and severe OSA (≥ 30/hour)[13]. A PSG not only provides the AHI, but also includes a hypnogram showing the sleep cycles, REM sleep, deep sleep, arousal index and awakenings (derived from electroencephalogram, electrooculogram and submental electromyogram). A PG provides the AHI without showing a hypnogram. As the PG does not measure sleep architecture as the PSG, the PG is limited in differentiating between sleep and wake time. Since during wake time the AHI is zero, the PG might underreport the AHI. Nevertheless, the PG still detects the clinically more relevant moderate and severe OSA. Therefore, the PG is used as a less expensive but still valuable alternative to PSG[12]. In case of moderate or severe OSA, continuous positive airway pressure (CPAP) therapy was prescribed. Data on P(S)G-AHI were collected from patient medical records and registered in an anonymous database. Clinical information was available, but index test results were not available to the readers of the reference test.

Checkme device description

The Checkme Health Monitor (BodiMetrics/Viatom Technology, Shenzen, People's Republic of China) is a biometrical device that amongst other things can be used as a sleep monitor for adults. The device consists of a finger pulse oxygen saturation (SpO_2) sensor attached to a monitor, which is held in place by a wristband. A researcher gave instructions on the use of the Checkme device and provided further

written instructions to take home. Patients used the Checkme at home for one night simultaneous with the P(S)G and returned the Checkme the following morning. In order for the data to be included in the study, we required at least 3.5 hours of good quality data. The raw data from the Checkme was downloaded and analyzed using Excel. Whereas clinical information was available, the results of the reference standard were not available to the readers of the index test. The Checkme has a sampling rate of 30 Hz. Invalid data, and data of the first 30 minutes were discarded, in an effort to include only 'sleeping' data. The recording period of the Checkme started 30 minutes after patients went to bed and stopped directly after waking up. Two different desaturations were defined, three and four percent drop in oxygen saturation from the pre-event baseline. Oxygen drop had to occur within a 1-min time frame, and last at least 10 seconds. The oxygen desaturation index (ODI) represents the number of oxygen desaturations occurring per hour during the recording period.

Statistical analyses

Power analysis showed that a minimum of 50 participants are necessary for two measurements (AHI and ODI) to provide a 95%-CI ± 0.1 for an estimated intra-class correlation coefficient (ICC) = 0.7. To compensate for approximately 25% of possible technical problems, we needed a total of 68 patients. Patient characteristics were described as means ± SD (depending on normality) for continuous variables or by percentages for categorical variables. ICC ± 95% confidence intervals (CI) was calculated to determine the agreement between P(S)G-AHI and Checkme-ODI, using a two-way mixed effects model for single measurement and absolute agreement. The ICC takes values in the range of zero (no agreement) to one (perfect agreement). ICC values less than 0.5 are considered 'poor', values between 0.5 and 0.75 'moderate', values between 0.75 and 0.9 'good', and values greater than 0.90 'excellent'. A high ICC means that the total variance within the data is rather explained by differences between individuals than by differences in the two measurement methods. We used the 95% limits of agreement approach (a.k.a. Bland & Altman plots) to assess the agreement between PSG-AHI and Checkme-ODI. The mean difference represents the systematic difference (bias) between the two measurement methods (P(S)G and Checkme). The 95% limit of agreement (mean difference ± 1.96 standard deviation) provides an estimate of how far apart the AHI and ODI values obtained by the P(S)G and Checkme were likely to be, respectively.

An AHI ≥ 15/hour is considered an important diagnostic cut-off value, as an AHI ≥ 15/hour is generally an indication for CPAP therapy. The diagnostic performance of the Checkme for AHI ≥ 15/hour was assessed using Receiver Operating Characteristic (ROC) curve analysis with corresponding area under the curve (AUC). The true positive rate (sensitivity) against the false positive rate (1-specificity) was plotted for different Checkme-ODI values.

A p-value of 0.05 was considered to indicate statistical significance. All data were analyzed by using SPSS 21.0 for Windows (SPSS Inc. Chicago Illinois, USA).

RESULTS

Study population

From October 2016 to March 2017, a total of 52 out of 68 patients completed the study (42 (81%) females, age 42 ± 5 years, Body Mass Index (BMI) 42.8 ± 5.0 kg/m^2). Sixteen patients returned the Checkme without any registered data. Two patients were excluded from further analysis due to a Checkme recording time less than 3.5 hours (possibly due to movement of the oxygen sensor). The remaining 50 patients had a mean recording time of 7.2 hours and were included for analysis. A total of 11 patients (22%) underwent pre-operative PG and 39 patients (88%) underwent pre-operative PSG. The prevalence of OSA (AHI ≥ 5/hour) was 72% in the present study. The numbers of patients with an AHI ≥ 5/hour, ≥ 10/hour, ≥ 15/hour or ≥ 30/hour were 36 (72), 22 (44), 18 (36) and 10 (20), respectively.

Agreement between Checkme-DI and PSG-AHI

The Checkme-ODI and P(S)G-AHI showed good agreement (ICC 0.85, 95%- confidence interval (CI) 0.75-0.91). The Bland-Altman plot (**Figure 1**) showed a mean difference of 1.72/hour between the Checkme-ODI and P(S)G-AHI, which means that the Checkme-ODI values were on average 1.72/hour lower than the P(S)G-AHI values. The limits of agreement estimated an interval of -16.74 to 20.18, which indicates that the Checkme may measure as much as 16.74/hour below and 20.18/hour above the P(S)G values. The Bland-Altman plot of the data showed a reasonably tight distribution in the lower values of P(S)G-AHI and Checkme-ODI. For values more than 15/hour, the absolute discrepancy between P(S)G-AHI and Checkme-ODI widened with a tendency for the Checkme to understate the values.

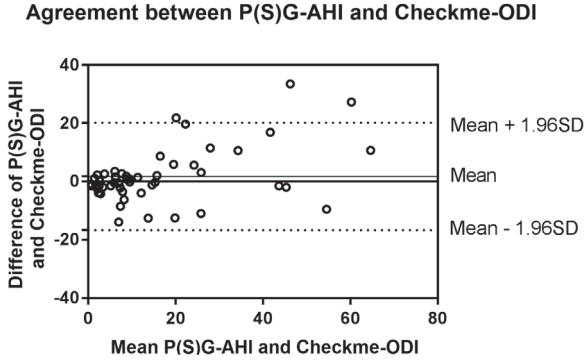


Figure 1 - Bland & Altman plot of P(S)G-AHI and Checkme-ODI.
Each circle represents a value measured by P(S)G-AHI and Checkme-ODI. Mean difference 1.72, LoA (-16.74 – 20.18). PSG = Polysomnography; AHI = Apnea–hypopnea index; ODI = Oxygen Desaturation Index

Diagnostic accuracy

Table 1 and 2 present validity measures of different cut-off values of the Checkme compared with different cut-off values of simultaneous P(S)G. Figure 2 displays the ROC-curve of different cut-off values of the Checkme for P(S)G-AHI ≥ 15/hour. Figure 2 displays the ROC-curve of different cut-off values of the Checkme for P(S)G-AHI ≥ 5/hour. The best cut off value was for 3%-ODI of the Checkme for an P(S)G-AHI ≥ 15/hour. The AUC value expressed by the ROC curve was 0.95 (95%-CI: 0.89-1.00, $p < .001$). For exclusive diagnosis (screening) the sensitivity and the negative predictive value (NPV) for the optimal cutoff value of Checkme-ODI≥ 9/hour were 100% and 100% respectively (Table 3). For definitive diagnosis, the specificity and the positive predictive value (PPV) for the optimal cutoff value of Checkme-ODI ≥ 9/hour were 69% an 64% respectively (Table 3).

Table 1 - Validity Measures of the Checkme compared with simultaneous P(S)G (cut-off value AHI ≥ 15/hour)

	AUC (95% CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR +	LR -
3%-ODI (9) ^	0.95 (0.89 – 1.00)	100	69	64	100	3.23	<.001
4%-ODI (3.35) ^	0.93 (0.86 – 0.99)	100	56	56	100	2.27	<.001
90%-ODI (1.05) ^	0.92 (0.85 – 0.99)	100	69	64	100	3.23	<.001
90%-min (2 min) ^	0.91 (0.83 – 0.99)	100	75	69	100	4	<.001

P(S)G = Poly(somno)graphy; AHI = apnea–hypopnea index; AUC = area under the receiver operating characteristic curve; CI = confidence interval;
PPV = positive predictive value, NPV = negative predictivevalue; LR = likelihood ratio; ODI = oxygen desaturationindex.
^ The paranthetical value represents the optimal cut-off value

Table 2 - Validity Measures of the Checkme compared with simultaneous P(S)G (cut-off value AHI ≥ 5/hour)

	AUC (95% CI)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR +	LR -
3%-ODI (1.95) ^	0.91 (0.82 – 1.00)	100	29	85	89	1.41	<.001
4%-ODI (0.6) ^	0.90 (0.82 – 0.99)	100	21	83	88	1.27	<.001
90%-ODI (0.05) ^	0.87 (0.78 – .0.97)	100	14	75	100	1.16	<.001
90%-min (0.05) ^	0.82 (0.71 – .0.94)	100	7	73	100	1.08	<.001

P(S)G = Poly(somno)graphy; AHI = apnea–hypopnea index; AUC = area under the receiver operating characteristic curve; CI = confidence interval;
PPV = positive predictive value, NPV = negative predictivevalue; LR = likelihood ratio; ODI = oxygen desaturationindex.
^ The paranthetical value represents the optimal cut-off value

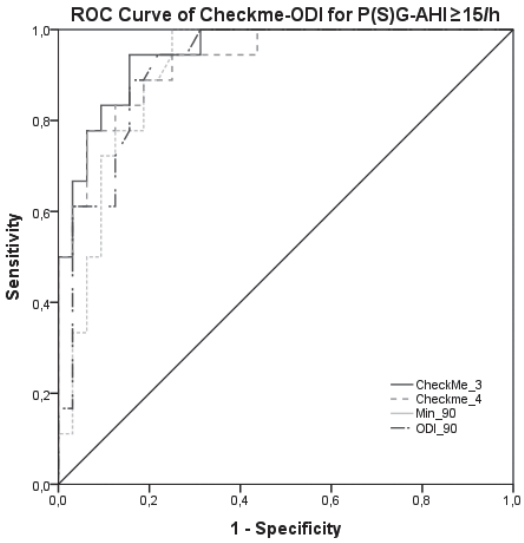


Figure 2 - Receiver operating characteristic curve of Checkme-ODI for P(S)G-AHI ≥ 15/hour 3%-ODI: Area under the curve: 0.95; 95% confidence interval: 0.98-1.00; P < 0.01; 4%-ODI: Area under the curve: 0.93; 95% confidence interval: 0.86- 0.99; P < 0.01.; 90%-ODI: Area under the curve: 0.92; 95% confidence interval: 0.85- 0.99; P < 0.01. 90%-min: Area under the curve: 0.91; 95% confidence interval: 0.83- 0.99; P <0.01.
PSG = Polysomnography; AHI = Apnea–hypopnea index; ODI = Oxygen Desaturation Index

Table 3 - Cross tabulation of the Checkme results by results of the P(S)G

	P(S)G-AHI ≥ 15/hour	P(S)G-AHI < 15/hour	
Checkme-ODI ≥ 9/hour	18	10	28
Checkme-ODI < 9/hour	0	22	22
Total	18	32	50

P(S)G = Poly(somno)graphy; AHI = Apnea–hypopnea index; ODI = Oxygen Desaturation Index

DISCUSSION

In this study we found good agreement between the Checkme and the gold standard PSG as expressed by the ICC (ICC 0.85, 95%-CI 0.75– 0.91). We demonstrated a small systematic difference between the P(S)G-AHI and the Checkme-ODI. For mean values of circa 15 or less the distribution of the Bland-Altman plot was sufficiently narrow, which means that the Checkme and the P(S)G may be essentially equivalent in these values. The limits of agreement got wider in higher values, which means that the bias between the Checkme and the P(S)G is larger as the severity of OSA increases. The Checkme cannot completely replace the P(S)G, yet the Checkme may be useful as a screening tool to rule out moderate and severe OSA.

To be applicable as a screening tool, the Checkme should have a high sensitivity with an acceptable specificity. At the cutoff value of ODI ≥ 9/hour, the Checkme showed to be highly sensitive in excluding moderate and severe OSA, specificity was acceptable. Patients with a Checkme-ODI < 9/hour could have been safely excluded from having clinically significant OSA (moderate and severe OSA), patients with a Checkme-ODI ≥ 9/hour should have undergone a P(S)G before bariatric surgery. No screening tools (devices, questionnaires, clinical prediction models) in bariatric surgery patients have reached this sensitivity of 100%[1,5-10]. A lower sensitivity would not be satisfactory, since some patients with clinically significant OSA are consequently not treated as they should. These patients will not be monitored postoperatively, and/or prescribed CPAP, which is associated with an increased risk for perioperative and postoperative complications.

In present study 42% of the patients had a Checkme-ODI value lower than 9/hour, which means that this percentage of the patients may not require an additional and costly sleep study. In morbidly obese patients screened by the STOP-Bang questionnaire, only 5% could have been saved a PSG. In previous studies approximately two-third of the bariatric surgery patients did not have moderate-to-severe OSA[2,12]. The 100% sensitivity with acceptable specificity found in this study, combined with a significant portion of patients without moderate-to-severe OSA provides the opportunity to screen patients. We propose to screen patients with the Checkme and refer only patients that are likely to have moderate-to-severe OSA patients for more extensive sleep study.

The Checkme is not resource- and budget intensive and may result in significant savings. Use of the Checkme may bypass sleep study waiting lists. Patients were instructed and furthermore provided with written and video instructions. Despite these extensive instructions, 16 out of 68 (24%) patients returned their devices without any data recorded. Although we decreased the number of patients with empty devices in the beginning of the study by more thorough instructions, we still had some patients with empty devices at the end of the study. We could not reconstruct whether this was due to technical problems of the Checkme or due to mistakes by patients. Yet, in daily practice, if necessary, patients could obviously use the Checkme an extra night.

The main limitation of present study is that not all patients underwent PSG due to organizational problems. We intended to perform a PSG in all patients who participated in the study, however time until surgery would have been constrained by limited availability of the PSG. Patients who underwent a PG or a PSG were separately assessed in subgroup analysis to evaluate effects of the diagnostic performance of the Checkme. No evidence was found for inconsistency of the results, which means that the results of present study were minimally influenced by the PG performed in a minority of the study population. The Checkme-ODI was systematically lower than the P(S)G-AHI. Similar to the PG, the Checkme cannot make a distinction between wake time and sleep time. The Checkme-ODI is based on the total recording time including wake time, whereas the AHI of the PSG is only based on the total sleep time during recording time. The Checkme-ODI may be influenced by the total wake time. Nevertheless, the Checkme will still detect the clinically relevant moderate and severe forms of OSA. Another limitation of the Checkme is that it cannot measure sleep position and, therefore, cannot make the distinction between supine and non-supine position. In this study, we cannot determine to what extent the Checkme will miss patients with a high AHI while sleeping in supine position.

This study was conducted in a single center with a relatively homogenous patients in terms of high probability of OSA. Obesity increases intermittent desaturations due to fat deposits in the upper airway region and decreased lung volume[14]. We hypothesize that the performance of the Checkme measuring the desaturation index is better in the bariatric population compared to the general population. The Checkme should be further validated in a larger multicenter cohort in the bariatric population and, furthermore, with a greater sample size of patients with an AHI $\geq$ 15/hour to detect the variability between the P(S)G and the Checkme in these OSA severity categories.

CONCLUSION

The Checkme cannot replace the PSG, but can be used as a valid screening tool to rule out moderate and severe OSA in bariatric surgery patients who present for preoperative evaluation. In our population, 42 % of the patients could have been withheld an extensive sleep study, using the Checkme data.

Acknowledgments | We would like to acknowledge BodiMetrics for supplying the Checkme pro for this study.

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Is fear for postoperative cardiopulmonary complications after bariatric surgery in patients with obstructive sleep apnea justified? A systematic review

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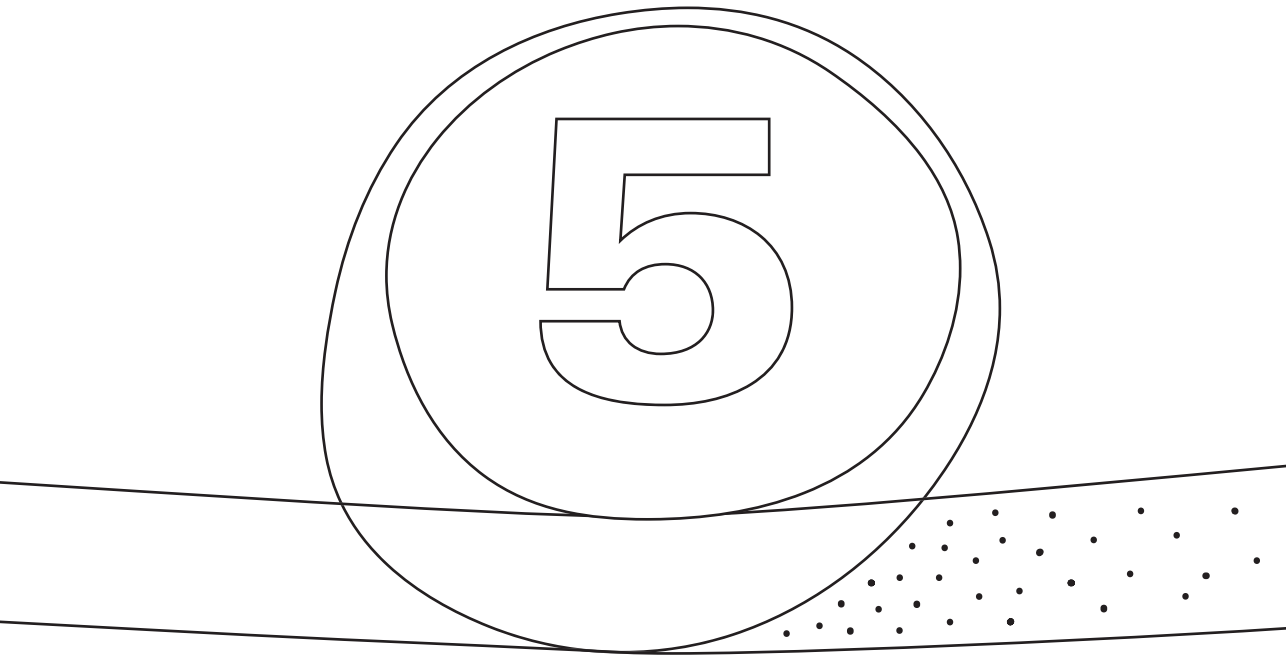

ABSTRACT

Introduction: To evaluate the influence of obstructive sleep apnea (OSA) on postoperative cardiopulmonary complications in bariatric surgery patients.

Methods: PubMed, Embase and the Cochrane central register databases were searched. The PRISMA statement was used for reviewing.

Results: Thirteen studies were included (n=98,935). OSA was documented in 36,368 (37%) patients. The cardiopulmonary complication rate varied between 0.0%-25.8%; no clear association with OSA was found (rate 0.0%-18%), possibly due to optimized situations such as continuous positive airway pressure (CPAP). OSA appeared to be no independent risk factor for Intensive Care Unit (ICU) admission, death or longer length-of-stay (LOS) in most studies.

Conclusion: Overall, presented data showed no clear association of OSA with cardiopulmonary morbidity, ICU admissions, mortality and LOS after bariatric surgery. Although this questions the justification of admitting OSA patients to the ICU, future studies are required investigating the effect of monitoring strategies and optimizing treatments including CPAP use.

INTRODUCTION

Obesity is a global health problem. It affected more than one-third of adults in the US in 2011-2012[1]. Since the incidence of obesity has nearly doubled since 1980[2], this has led to an increase of bariatric surgical procedures. With an incidence of 70-80%, obstructive sleep apnea (OSA) is one the highest accompanying comorbidities in bariatric surgery patients[3-4].

Bariatric surgery, which is generally accepted and proven to be safe in many cohorts[5-8], leads to reduction or even curation of OSA[9-10]. However, there are concerns regarding the perioperative management of bariatric surgery patients with OSA as serious cardiopulmonary complications, including respiratory failure, cardiac arrest and death have been reported[11-13]. Still, consensus is lacking regarding the postoperative care of these patients. Existing guidelines for postoperative care are based primarily on expert opinion rather than on scientific evidence[14].

To the authors' knowledge, this is the first systematic review providing an overview of the evidence of the postoperative cardiopulmonary complication rate of bariatric surgery patients and the influence of OSA. With the enormous increase in the performance of bariatric surgery and the high incidence of OSA among these patients, this review is believed to be a subject of interest as it concerns the perioperative safety of the majority of bariatric surgery patients.

The primary objective was to evaluate the postoperative cardiopulmonary complication rate in bariatric surgery patients, whether these complications are commonly associated with OSA in the postoperative setting and what interventions were required. Secondary objectives were to determine whether the presence of OSA influenced the mortality and overall complication rate, Intensive Care Unit (ICU) admissions or length of stay (LOS) after bariatric surgery. Due to heterogeneity of included studies, no meta-analysis was feasible.

METHODS

Literature Search

Studies were identified by searching both PubMed and Embase databases and the Cochrane central register for controlled trials. The last search was run on 25-09-2014 using the keywords [Bariatric Surgery; Obstructive Sleep Apnea; Continuous Positive Airway Pressure; Postoperative Complications; Length of Stay; Intensive Care Unit]. After Mesh terms and free text words were combined for this search, references of included studies were cross-checked.

Study Selection and Data Extraction

Study selection and data extraction was done according to the PRISMA statement[15]. Full text articles, written in English and investigating direct and 30-day post-bariatric (cardio)pulmonary status, including influence of OSA, were included in this review. Records excluded from the review were other reviews with a different end point, case reports, letters and articles that were not available in full text, not describing research or written in a different context. Eligibility assessment, data extraction and quality scoring was done independently by two reviewers (CdR and UC), who discussed and resolved differences of opinion during a consensus meeting. Extracted data were: [1] baseline characteristics (**Table 2**), [2] definitions regarding diagnosis and therapy of OSA + results of Continuous Positive Airway Pressure (CPAP) use and compliance (**Table 3**), [3] primary (cardiopulmonary complications and interventions) and secondary (overall complications, deaths, ICU admissions, LOS in ICU, LOS in post anesthesia care unit (PACU) and LOS in hospital) outcome measures. Quality rating of included studies was done according to the Cochrane Collaboration's tool for assessing risk of bias[16]. Studies with prospective consecutive collected data providing retrospective analysis were qualified as being prospective.

RESULTS

Included Studies

The search process and study selection are displayed in a flowchart (**Figure 1**). Literature search provided 1797 publications, of which 1635 were written in a different context and therefore primarily discarded. After excluding 87 of 163 selected abstracts, 76 articles were read in full text. Of these articles, thirteen were considered suitable for this review. Since no additional articles were found by cross-checking references, thirteen studies were analyzed and critically appraised (**Table 1**).

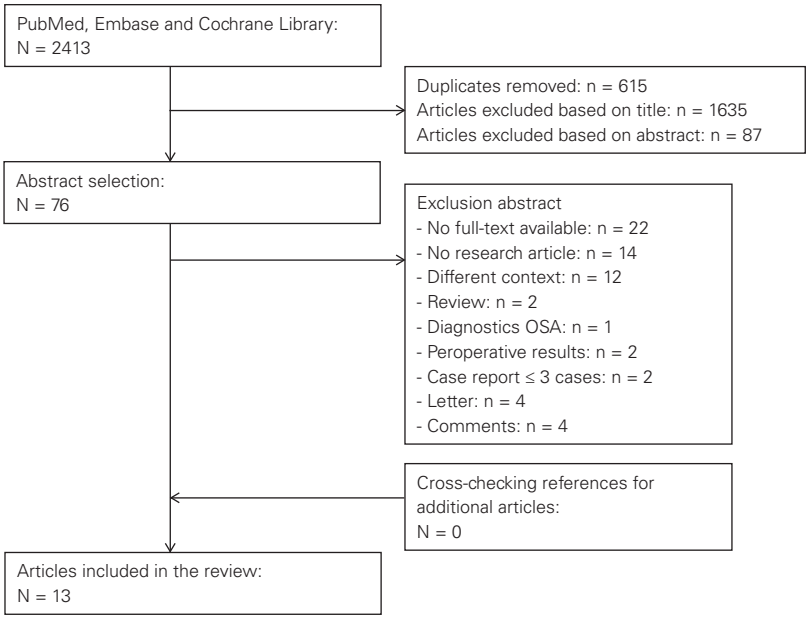

Figure 1 - Flowchart of inclusion/exclusion process

Table 1 - Quality of included studies

Publication	Prospective or retrospective consecutive data	Statistical method described	Comparability	Low risk of selection bias	Low risk of performance bias	Low risk of detection bias	Low risk of attrition bias	Total
Ahmad 2008 [17]	Prospective	+	+	+	-	-	+	5
El Shobary 2008 [23]	Retrospective	+	-	+	-	-	+	3
Gallagher 2010 [18]	Prospective	-	-	-	+	+	+	4
Grover 2010 [24]	Retrospective	+	-	+	-	-	+	5
Hallowell 2007 [19]	Prospective	+	+	-	-	-	+	6
Helling 2004 [25]	Retrospective	+	-	+	-	-	+	4
Huerta 2002 [20]	Prospective	+	-	+	+	+	+	6
Jensen 2008 [21]	Prospective	+	+	+	-	-	+	4
Meng 2010 [26]	Retrospective	+	-	-	+	+	+	5
Kurrek 2011 [29]	Retrospective	+	-	-	+	-	+	4
Mokhlesi 2013 [27]	Retrospective	+	-	+	-	-	+	4
Shearer 2013 [22]	Prospective	+	-	+	+	-	+	5
Weingarten 2011 [28]	Retrospective	+	-	+	-	+	+	5

Prospective = 1 point, retrospective = 0 points + = 1, - = 0, maximum points is 7.

Study characteristics

Six prospective[17-22] and seven retrospective[23-29] studies were included, providing a total of 98,935 bariatric surgery patients (80% female, mean BMI ranging from 48 to 56; **Table 2**). Definitions regarding diagnosis and therapy of OSA are displayed in **Table 3**. Diagnosis of OSA was documented in 36,368 (37%) patients. No study, except Ahmad et al.[17] and Hallowell et al.[19], performed standard polysomnography (PSG) in their study groups. While some studies used selective PSG based on clinical criteria, the Epworth Sleepiness Scale (ESS)/Berlin/STOP-BANG questionnaires or clinical suspicion, others do not describe their diagnostic tool(s) or criteria when to perform PSG. Definition of OSA was mentioned in four studies[23-24;28-29], whereas indication of CPAP therapy was described in two studies[22;24], differing in indication. One study provided the results between different OSA severities[28]. One study defined CPAP compliance[19], whereas none of included studies provided data on CPAP compliance. Influence of OSA on postoperative outcome was reported in seven studies[17-18;21-22;24;27-28], whereas three studies analyzed outcomes with and without CPAP therapy[20-21;26]. Two studies compared ICU admissions in different cohorts[19;23] and one study described outcomes of patients admitted to the ICU[25].

Postoperative hypoxemia

Six studies reported postoperative hypoxemia[17-18;23-24;26;29]. Kurrek et al. (n=2370) investigated desaturations in the early postoperative period, including during extubation and PACU stay. Overall, 746 (40%) OSA patients experienced saturation levels below 93% after surgery. This occurred in 222 (30%) patients in the overall study population. However, no statistical comparison between these groups was available[29]. Two studies showed low postoperative desaturation rates. Grover et al. (n=650) optimized patients with oxygen and incentive spirometer. Postoperatively, a single case of hypoxia occurred in both OSA and non-OSA groups[24]. El Shobary et al. (n=250) found a desaturation rate of 2% in OSA patients (apnea-hypopnea-index (AHI) > 5/hour)) who were all admitted to the ICU when BMI was more than 50 kg/m² and age above 40 years[23]. In agreement with Grover et al., no difference was found between OSA patients, who were monitored at an ICU, and non-OSA patients, who were admitted to a general surgical ward in the study of Ahmad et al. (n=40)[17]. While preoperatively prescribed CPAP therapy was applied postoperatively, all subjects received 3L/min supplemental oxygen and were continuously monitored. In a pilot study (n=13) where continuous oximetry was blinded and silenced, all patients experienced, mostly multiple, episodes of SpO2 less than 90% lasting for more than 30 seconds. OSA was described in ten (77%) patients[18].

Comparison of desaturation rates between CPAP and no-CPAP patients was done in two studies[17;26]; however, both studies provided no information regarding CPAP indication and compliance.

Cardiopulmonary complications and interventions

Twelve studies provided their (cardio)pulmonary complication rate, varying between 0.0%-25.8%[17-24;26-29]. Meng et al. found that 25.8% of the patients developed postoperative hypertension requiring intravenous antihypertensive medication. No association with OSA was established since it was more prevalent in the non-OSA group (29% versus 18%, $p = 0.01$)[26]. All other studies had a complication rate varying between 0.0%-7.4%[17-24;27-29]. Complications varied in severity from hypertension and pneumonia to respiratory failure and atrial fibrillation.

Overall, a low incidence of pulmonary infections was found. Ahmad et al. (n=40) presented one patient in the non-OSA group with aspiration pneumonitis, and no complications in the OSA group[17]. Shearer et al. (n=192) only reviewed OSA patients of which one (0.5%) experienced a chest infection[22]. In the study by Jensen et al. (n=1095), pneumonia occurred in four OSA patients and five non-OSA patients (1.4% versus 0.6%; p = ns)[21]. While Mokhlesi et al. (n=91,028) found less pneumonias (0.6% versus 1%, $p < 0.01$) and tracheostomy placements (0.08% versus 0.13%, $p = 0.02$) in the OSA group, these patients had an increased number of respiratory failure (1.8% versus 1.5%, $p < 0.01$) and atrial fibrillation (1.8% versus 1.2%, $p < 0.01$). The number of coronary procedures was similar in both groups (0.1%)[27].

Hallowell et al. (n=890) published results of two cohorts differing in preoperative OSA diagnosing. In group one (n=572), that had selective OSA testing (based on clini-

Table 2 - Baseline characteristics, type of surgery, operative characteristics, apnea-hypopnea index

Author	N	Gender (F/M)	Age (year)	BMI (kg/m²)	OSA (n)	Monitoring level (n)	History of cardio-pulmonary disease	Lap/ Open	Type of surgery (n)	Anesthetic (A)/ surgery (S) time (min)	Sed
Ahmad 2008 [17]	40	32/8	43 ± 10	50 ± 9	31	ICU: 31 SW: 9	HT: 11 CAD: 1 PHT: 6	Lap	GBP: 23 GB: 11	S: OSA: 170 S: non-OSA: 140	+
El Shobary 2008 [23]	250	192/58	'04: 38.0 ± 8.5 '05: 37.7 ± 9.0	'04: 51 ± 10 '05: 53 ± 10	'04: 53 '05: 32	ICU '04: 70 '05: 13 SW '04: 52 '05: 115	HT: 93 CAD: 7 HL: 19 Asth: 55	Lap	GBP: 250	A: '04: 143 A: '05: 135	-
Gallagher 2010 [18]	13	11/2	44 ± 4	48 ± 2	10	SW: 13	-	-	RYGBP: 13	-	-
Grover 2010 [24]	585	492/93	OSA: 43.9 ± 9.3 Non-OSA: 41.8 ± 9.6	OSA: 47.9 ± 6.1 No-OSA: 47.5 ± 5.6	217; 148 severe	SW: 585	Asth: 112 COPD: 9	Lap	GBP: 585	-	+
Hallowell 2007 [19]	890	773/117	G1: 43 ± 1 G2: 44 ± 1	G1: 51.9 ± 0.3 G2: 49.3 ± 0.5	453	ICU G1: 32 G2: 11	HT: 365	Lap: 164 Open: 726	RYGBP: 890	-	-
Helling 2004 [25]	250	192/58	43.6 ± 10.6	56 ± 10.6	-	ICU: 75 SW: 175	Pulm: 123	Open	VBG: 15 RYGBP: 235	S: 180	-
Huerta 2002 [20]	1067	847/230	42.3 ± 0.3	53.6 ± 0.3	420	-	-	Open	RYGBP: 1067	-	-
Jensen 2008 [21]	1095	929/166	OSA+CPAP: 47 OSA-CPAP: 44 No-OSA: 43	OSA+CPAP: 49 OSA-CPAP: 47 No-OSA: 49	284	Telemetry ward/ ICU	-	Lap	RYGBP: 1095	-	-
Meng 2010 [26]	357	281/76	46.5 ± 0.4	51.5 ± 0.3	146	ICU: 15	HT: 92	Lap	RYGBP: 357	A: 216	+

Table 2 - Baseline characteristics, type of surgery, operative characteristics, apnea-hypopnea index (continued)

Author	N	Gender (F/M)	Age (year)	BMI (kg/m²)	OSA (n)	Monitoring level (n)	History of cardio-pulmonary disease	Lap/ Open	Type of surgery (n)	Anesthetic (A)/ surgery (S) time (min)	Sed
Kurrek 2011 [29]	2370	1947/ 424	46 ± 11	42.7 ± 7.7	746	Direct discharge outpatient basis after PACU discharge: 2370	HT: 732 Asth: 305	Lap	GB: 2370	A: 83 ± 23 (all patients) A: 85 ± 22 (OSA)	+
Mokhlesi 2013 [27]	91028	72822/ 18206	44.2	-	33196	-	-	-	-	-	-
Shearer 2013 [22]	192	100/92	46	52	192	Level 2: 192	-	Lap	LAGB: ? RYGBP: ? SG: ? DS: ?	-	+
Weingarten 2011 [28]	797	591/206	46.6 ± 10.8	49.5 ± 9.4	618; 244 severe	ICU: 130 IMCU: 556 SW: 111	HTN: 439 CVD: 126 Pulm: 221	Lap: 355 + Open: 442	-	A: 289	-

Asth = Asthma; CAD = Coronary Artery Disease; CVD = Cardiovascular disease; G = Group; GB = Gastric banding; GBP = Gastric bypass; HL = Hyperlipidemia; HT = Hypertension; ICU = Intensive Care Unit; IMCU = Intermediate Care Unit; Lap = Laparoscopic Procedure; Min = Minimum; Open = Open Procedure; Preop = Preoperative period; Pulm = Pulmonary co-morbidity; PHT = Pulmonary Hypertension; RYGBP = Roux-and-Y Gastric Bypass; Sed = Sedatives (morphine/fentanyl); SW = Surgical Ward; Tot = Total; VBG = Vertical Banded Gastroplasty

Table 3 - Definitions regarding diagnosis and therapy of OSA + results CPAP use and compliance

Author	Diagnostic OSA tool (n)	Definition OSA	Indication for CPAP therapy	Definition CPAP compliance	CPAP (n)	Results CPAP compliance
Ahmad 2008 [17]	All patients: PSG (40) + Berlin (40)	-	-	-	Preop: 8 Postop: 6	-
El Shobary 2008 [23]	PSG (55)	OSA = Apnea index > 5/h (i.e. AHI > 10/h) Severe OSA = OSA requiring CPAP therapy	-	-	Preop '04: 15 Preop '05: 16 Postop '04: 6 Postop '05: 5	-
Gallagher 2010 [18]	All patients: ESS (13); When ESS ≥ 6 à PSG + CPAP titration	-	-	-	Preop: 8 Postop: 8	-
Grover 2010 [24]	All patients: ESS; When ESS ≥ 10 à formal sleep apnea evaluation, often including PSG (217)	RDI (i.e. AHI) 5-14.9 = mild; 15-30 = moderate > 30 = severe	Postop: When oxygen saturation < 90% despite nasal oxygen or on patient request	-	Postop: 42 0%: mild 20%: moderate 22%: severe	-
Hallowell 2007 [19]	< 2004: selective PSG based on clinical criteria: positive ESS, loud snoring, daytime sleepiness or clinical suspicion > 2004: PSG (318)	-	-	6h/day	-	-
Helling 2004 [25]	-	-	-	-	-	-
Huerta 2002 [20]	-	-	-	-	Preop: 159 Postop: 159	-
Jensen 2008 [21]	-	-	-	-	Preop: 144 Postop: 0	-
Meng 2010 [26]	PSG (146)	-	-	-	Preop: 102 Postop: 102	-
Kurrek 2011 [29]	-	High risk for OSA if: CPAP preoperatively or history of at least three STOP-BANG criteria	-	-	Preop: 357 Postop: 357	-

Table 3 - Definitions regarding diagnosis and therapy of OSA + results CPAP use and compliance (continued)

Author	Diagnostic OSA tool (n)	Definition OSA	Indication for CPAP therapy	Definition CPAP compliance	CPAP (n)	Results CPAP compliance
Mokhlesi 2013 [27]	Diagnosis OSA according to ICD-9 codes	-	-	-	CPAP/NIV during hospitalization: 1.9%	-
Shearer 2013 [22]	-	-	Postop: saturation < baseline level despite increase FiO2 or for personal comfort	-	Preop: 192 Postop: 4	-
Weingarten 2011 [28]	All patients with suspected OSA were referred for PSG (797)	No OSA = AHI ≤ 4 Mild = 5-15 Moderate = 16-30 Severe ≥ 31	-	-	Preop: 654	-

OSA = Obstructive Sleep Apnea; CPAP = Continuous Positive Airway Pressure; PSG = Polysomnography; AHI = Apnea Hypopnea Index; RDI = Respiratory Disturbance Index; Berlin = Berlin questionnaire; ESS = Epworth Sleepiness Scale; Preop = Preoperative period; Postop = Postoperative period

cal suspicion), 32 (6%) patients required ICU admission, of which eleven (34%) due to respiratory reasons. OSA was diagnosed in ten out of 32 patients, of which four developed respiratory distress. In the second group (n=318), that had mandatory OSA testing, one out of eleven ICU admissions was related to respiratory problems due to CPAP noncompliance. Of these eleven admissions, ten were preoperative diagnosed with OSA[19]. Three other studies found no cardiopulmonary complications[18;20;29].

Three studies attempted to examine the correlation of OSA severity with postoperative pulmonary complications[21;23;28]. Within the patients admitted to the ICU, three patients (4%) in 2004 (BMI ≥ 50; AHI > 5/hour) and three (23%) in 2005 (BMI ≥ 60; OSA, requiring CPAP therapy) developed respiratory problems. Three patients (1.2%) required an intervention, including pressure support ventilation (n=2) or mechanical ventilation (MV; n=1). No statistical difference was found between both cohorts[23]. In addition, pulmonary complications that occurred in 59 patients (7.4%) were not associated with OSA severity in the study of Weingarten et al.[28]. In the manuscript of Jensen et al., no significant difference was detected between non-OSA patients, OSA patients without CPAP and OSA patients with CPAP treatment[21].

Reintubations were mentioned in six studies, reporting an 0.0%-4.8% incidence in their overall study population. Reintubations in the OSA group varied from 0.0%-5.6%; in the non-OSA group 0.0%-11%. Mokhlesi et al. found a higher percentage of reintubations in the OSA group (5.6% versus 1.2%; $p < 0.01$)[27]. Three studies found no difference in reintubation rates between OSA and non-OSA patients[17;21;29]. Likewise, one study found no difference between CPAP and non-CPAP patients[26]. Weingarten et al. reported 17 reintubations (2%; 1 non-OSA and 16 OSA patients). No comparison was made statistically[28].

ICU admissions

In addition to Hallowell et al., six additional studies reported ICU admissions. One study reported ICU admissions for pulmonary reasons. Although not statistical significant, two (2%) patients treated with- and thirteen (5%) without CPAP were admitted to the ICU in the study by Meng et al.[26]. Three studies reported no cardiopulmonary related ICU admissions[22-24]. In multivariable analysis, preoperative pulmonary comorbidities, including OSA, hypoventilation syndrome and reactive airway disease, were no determinant for ICU need or prolonged MV[25]. Weingarten et al. reported the postoperative monitoring level without describing the reasons for admission to the ICU, intermediate care unit or regular nursing floor. For this reason, these results were not useful for this review[28].

Mortality rate

Mortality was reported in seven studies. An overall mortality rate of 0.3% was described by Hallowell et al.[19], whereas a difference between non-OSA (0.3%) and OSA (0.1%) groups was found by Mokhlesi et al.[27]. In the study by Weingarten et al., three patients (0.4%) died due to pulmonary embolism (n=1) or sepsis (n=2) in the 30-day postoperative period[28]. Four other studies reported no deaths[21-22;24;29].

Overall postoperative complications, length of stay

Grover et al. found no difference in overall complications between OSA and non-OSA patients[24]. While one study showed no complications[21], three studies reported a complication rate without providing a correlation with OSA[19;28-29]. Without a non-OSA comparison group, Shearer et al. reported an anastomotic leakage incidence of 2.4% in OSA patients[22]. Huerta et al. (n=1067) reported leakages in 15 bariatric surgery patients (1.4%), in which no correlation with CPAP use was found[20].

Total LOS in hospital was longer in patients who required ICU admission[25], in the 2005 cohort[23] and in one non-OSA group (7.10 days instead of 5.78 days in OSA group)[27]. No differences in LOS in hospital were found between all other OSA/non-OSA groups[17;22;24] and between CPAP/non-CPAP groups[21]. In addition, LOS was not associated with OSA severity[28].

Table 4 - Outcomes investigated in the included studies

		Outcomes						
Study design		Postoperative hypoxemia	Cardio- and or pulmonary complications	Interventions	ICU admission	Overall complications	Deaths	LOS hospital
Ahmad 2008 [17]	Prospective	+	+	+	-	-	-	+
El Shobary 2008 [23]	Retrospective	+	+	+	+	-	-	+
Gallagher 2010 [18]	Prospective	+	+	-	-	-	-	-
Grover 2010 [24]	Retrospective	+	+	-	+	+	+	+
Hallowell 2007 [19]	Prospective	-	+	-	+	+	+	+
Helling 2004 [25]	Retrospective	-	-	+	+	-	-	+
Huerta 2002 [20]	Prospective	-	+	-	-	+	-	-
Jensen 2008 [21]	Prospective	-	+	+	-	+	+	+
Meng 2010 [26]	Retrospective	+	+	+	+	-	-	-
Kurrek 2011 [29]	Retrospective	+	+	+	-	+	+	-
Mokhlesi 2013 [27]	Retrospective	-	+	+	-	-	+	+
Shearer 2013 [22]	Prospective	-	+	-	+	+	+	+
Weingarten 2011 [28]	Retrospective	-	+	+	+	+	+	+

"+" = item reported in study; "-" = item not reported in study
LOS = Length of Stay; ICU = Intensive Care Unit

DISCUSSION

The aim of this review was to evaluate the postoperative cardiopulmonary complication rate after bariatric surgery and its association with OSA. The overall cardiopulmonary complication rate varied between 0.0% and 25.8%; no clear association with OSA patients was found.

In the analyzed thirteen studies, OSA was diagnosed in 36,368 patients (37%), of which 33,196 were included in one study[27]. This rate is significantly lower than the 70-80% reported in literature[3], and implicates underdiagnoses of OSA. Although Ahmad et al. and Hallowell et al. routinely performed PSG in their study groups, in all other studies, PSG's were only performed in case of high clinical suspicion on OSA, e.g. based on clinical criteria, ESS/Berlin/STOP-BANG questionnaires or clinical suspicion otherwise. Due to inconsistent literature, no definite conclusion regarding the most accurate available OSA questionnaire is drawn[30]. Existing clinical scoring schemes are not accurate enough to replace PSG in the evaluation of OSA[31]. This strongly suggests that the non-OSA groups analyzed in this review may have included many not diagnosed OSA patients.

Postoperative desaturations

In active monitored OSA patients, the incidence of postoperative hypoxia varied between 0.5% and 40%. The high incidence of 40% occurred during the early postoperative period, including extubation and PACU stay. These results imply that OSA patients must be well monitored directly after bariatric surgery. In other active monitored studies, the incidence of desaturations was low. Although a trend was seen towards more desaturations in OSA patients in some studies, others found no difference between OSA and non-OSA patients. These controversial results are likely to be caused by optimized care, including supplemental oxygen, CPAP therapy or ICU monitoring. In addition, included studies are heterogenic regarding OSA diagnostic tools, definition and indication for CPAP treatment. These limitations make it more complex to specify which OSA patients experienced desaturations and were treated with CPAP. Although two studies compared outcomes between patients with- and without CPAP treatment, no information regarding definition and compliance of CPAP was given. While this review therefore cannot answer the question whether CPAP reduces the desaturation and complications risks in OSA patients, in general, CPAP improves oxygenation[26], has shown reduction of lung volume loss directly after extubation[32] and minimizes pulmonary complications after bariatric surgery[33].

In addition, blinded and silenced monitoring revealed hypoxia in 100% of the patients. As one desaturation episode lasted for 21 (± 15) minutes and one patient experienced a low SpO2 of 75% ±8% without clinical alterations or suspicions, continuous monitoring may be recommended within bariatric surgery patients suffering from OSA, especially with the use of narcotic analgesics and patient care analgesia. Occasional measurements of vital parameters could miss transient and multiple

hypoxemic episodes without continuous monitoring[18]. Future studies are required to answer the question which specific OSA patients require which monitoring/therapy. Until then, continuous monitoring, either at a designated surgical ward or, when not available, MCU, for at least those with severe OSA would provide safe postoperative care.

Cardiopulmonary complications, interventions, ICU admissions

Overall, the incidence of severe cardiopulmonary related morbidity was very low. Although one study found significant differences between OSA and non-OSA patients, the study group was enormous (n = 98.028), whereas the complication rates were very low (≤ 1.8%)[27]. This means that within large study populations, small numbers of complications are likely to be significant, of which level is not clinical relevant. Moreover, other studies showed no difference in cardiopulmonary complications between clinically diagnosed, but not always PSG confirmed OSA and non-OSA groups[17;21;24;28].

One of the interventions that might require ICU admission due to cardiopulmonary complications is reintubation. While few (emergent) reintubations were reported, these results show a trend of an increased intervention risk towards OSA patients and those not treated with CPAP. Although this small incidence show that routine ICU admission is not required, an emergent intervention must be available for such rare incidents.

In one study group (n=318), that had mandatory OSA testing, one out of eleven ICU admissions was related to respiratory problems due to CPAP noncompliance. Of these eleven admissions, ten were diagnosed with OSA preoperatively[19]. These results imply that ICU admission was not a consequence of OSA. All other studies show that OSA is no independent risk factor for ICU admission.

Overall complications, mortality, length of stay

The only study comparing overall complication rate between OSA and non-OSA patients found no difference[24]. No study found an increased mortality rate due to OSA[29;34]. The presence and severity of OSA appeared no predictor for LOS in hospital and LOS in ICU. However, there might be undiagnosed and untreated OSA patients in the non-OSA group introducing bias to these results and conclusions.

As already laid out above, this systematic review has several limitations primarily based on its included studies. Although one prospective study calculated a sample size, no study in this review was a randomized controlled trial. All studies were prospective observational or retrospective. Meta-analysis was no option, due to both quality of included studies and heterogeneity, which was a result of different study groups, definitions of OSA and CPAP indication, diagnostic tools, outcome measures, such as hypoxemic episodes, and postoperative care, concerning duration of MV, moment of extubation, CPAP therapy and compliance, supplemental oxygen and PCA. **Table 3** illustrates not only heterogeneity, but also the lack of data

regarding definitions. Additionally, it could be hypothesized that OSA severity has an influence on the postoperative cardiopulmonary outcome. However, only one of the included study examined these outcomes between no- (AHI 0-5/hour), mild- (AHI 5-15/hour), moderate- (AHI 15-30/hour) and severe (AHI > 30/hour) OSA. For future studies, it is recommended to perform mandatory P(S)G prior to surgery and to not only evaluate the influence of OSA (AHI > 5/hour) on the postoperative outcome, but also the influence of OSA severity. Finally, none of included studies mentioned the supine AHI, which is relevant as the total AHI is composed of an AHI in left, right, supine and prone position[35]. In particular in mild to moderate OSA, many patients are positional as defined as having an AHI that is at least twice as high in supine position as in lateral position[36-37]. Since many bariatric surgery patients sleep on their back directly postoperatively, in such cases the supine AHI might be more important that the total AHI.

CONCLUSION

Overall, the cardiopulmonary complication rate varied between 0.0% and 25.8%. No clear association with OSA (0.0%-18.0%) was found in this review. In addition, no clear association was found between OSA and cardiopulmonary related ICU admissions, mortality, overall complications and LOS in hospital after bariatric surgery. These results question the justification of routine admission of OSA patients to the ICU. However, results are influenced by optimized situations such as CPAP therapy, ICU monitoring and oxygen supplementation. As the true influence of OSA on postoperative cardiopulmonary outcome remains unknown due to these optimizations, large prospective studies providing standard preoperative P(S)G in all patients scheduled for bariatric surgery are required to investigate the reliable effect of monitoring strategies and optimizing treatments such as CPAP use on the postoperative course. These studies could provide protocols based on scientific evidence rather than experts opinions for the perioperative OSA management, including preoperative OSA screening and treatment. Until then, the authors advise continuous monitoring at a designated surgical ward, or MCU when not available, for at least those patients with severe OSA. Pre- and postoperative CPAP use is advised in patients with moderate and severe OSA. It can be concluded that presented data hold no support for the routine admission of all OSA patients to the ICU.

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Positional obstructive sleep apnea in bariatric surgery patients: risk factor for postoperative cardiopulmonary complications?

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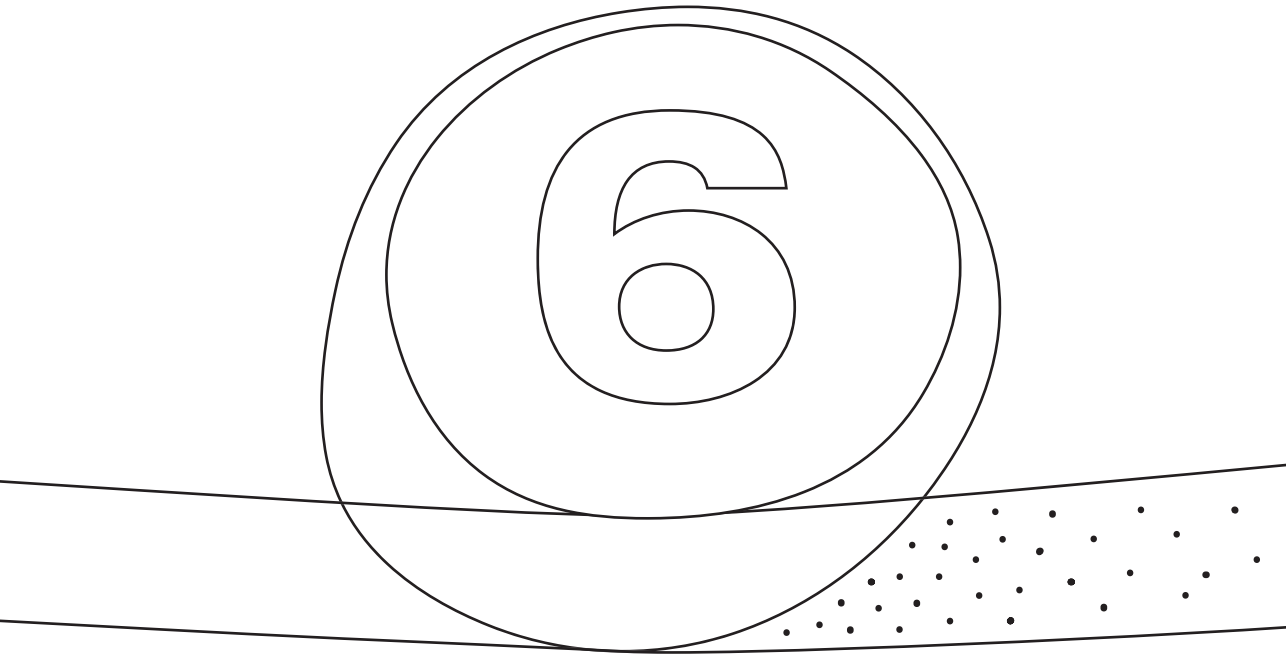

ABSTRACT

Introduction: Up to 80% of the bariatric surgery patients suffer from obstructive sleep apnea (OSA). Bariatric patients with moderate to severe OSA (apnea-hypopnea-index (AHI) ≥ 15/hour) are usually treated with continuous positive airway pressure (CPAP). This is not indicated in mild OSA patients (AHI < 15/hour). However, >50% of patients with mild OSA have positional-OSA (POSA); their AHI is at least twice as high in supine sleeping position than in other positions. Since many patients sleep in supine position for surgical safety reasons after bariatric surgery, evaluating the AHI in this position might be more relevant in this group. The aim of this study is to evaluate the postoperative cardiopulmonary complication rate in mild OSA patients with and without POSA. Secondary aim is to evaluate predictive factors for POSA.

Methods: A single-institute retrospective analysis was achieved with all consecutive patients who underwent primary laparoscopic Roux-en-Y gastric bypass or laparoscopic sleeve gastrectomy between 2006 and 2014. All patients with an AHI between five and fifteen were included. Postoperative complications were compared between POSA and non-POSA patients. Predictive factors were evaluated through uni- and multivariable logistic regression analysis.

Results: A total of 277 patients, 153 with and 124 without POSA, were included. After bariatric surgery, three patients (1.1%) experienced severe cardiopulmonary complications. No significant difference was found between POSA and non-POSA patients. In multivariable analysis, age and BMI were found to be negative predictors for POSA.

Conclusion: In terms of 30-day postoperative cardiopulmonary outcome, CPAP therapy is not indicated in mild (P)OSA patients scheduled for bariatric surgery.

INTRODUCTION

Morbid obesity is a problem of epidemic proportions. Worldwide, more than 340,000 bariatric surgical procedures, of which the majority included the laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic sleeve gastrectomy (LSG), were performed in 2011[1]. In the long term, bariatric surgery has shown to be the only effective therapy for weight reduction and improvement of comorbidities[2], such as obstructive sleep apnea (OSA). This comorbidity is highly prevalent in the bariatric population, reaching a prevalence of 70-80%[3-4]. Since OSA is associated with severe postoperative cardiopulmonary complications, such as respiratory insufficiency, cardiac arrest and death[5-7], preoperative diagnosis and, if necessary, treatment of OSA is recommended[5]. The diagnosis of OSA is established with polygraphy (PG), or polysomnography (PSG)[8], providing the apnea-hypopnea-index (AHI), in which the OSA severity is expressed. An AHI of 0-5/hour states no OSA, whereas scores of 5-15/hour, 15-30/hour and ≥ 30/hour state mild, moderate and severe OSA, respectively[5;9]. In case of moderate or severe OSA, continuous positive airway pressure (CPAP) therapy is prescribed[10]. This is generally not indicated in patients with mild OSA (AHI < 15/hour).

The total AHI is composed of an AHI in supine and non-supine, including lateral- and prone, position. Patients who have an AHI that is at least twice as high in supine as in non-supine position have positional OSA (POSA)[11]. The AHI is a significant predictor for POSA due to this ratio. Most of the patients with mild OSA are positional (> 50%)[12], while patients with moderate OSA and in particular with severe OSA, are mostly non positional; here the AHI is high in all sleeping positions[13]. This implies that patients with mild OSA, who are not treated with CPAP, are likely to have POSA, which may result in similar postoperative risks as moderate to severe non-positional OSA. Depending on their percentage of total sleep time (% TST) in supine position, it would be more logical to evaluate the AHI in this position as well. After surgery, the % TST in supine position might be even increased. Taken this in mind, POSA patients with a total AHI below fifteen might also require CPAP treatment.

The primary aim of this study is to evaluate the postoperative cardiopulmonary complication rate of mild OSA patients with and without POSA. The secondary aim is to evaluate predictive factors for POSA. It is hypothesized that POSA patients have an increased risk of developing postoperative cardiopulmonary complications that require treatment, when compared to non-POSA patients.

METHODS

Study design and study population

A retrospective study was performed with all consecutive patients who underwent bariatric surgery in our hospital between March 2006 and October 2014. All patients met the criteria for surgery, according to the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO)[14].

Patients who underwent a LRYGB or LSG were considered eligible for inclusion, whereas other bariatric procedures such as laparoscopic gastric banding (LAGB) or revisional surgery were excluded. Patients were included when poly(somno)graphy (P(S)G) data, concerning the AHI and % TST in different sleeping positions, were available and revealed a total AHI between five and fifteen, defining mild OSA. Consequently, all patients with an AHI below five or above fifteen or incomplete PG data were excluded from this study.

Evaluation obstructive sleep apnea

Preoperative P(S)G provided the AHI, in which the OSA severity is expressed. An AHI of 0-5/hour states no OSA, whereas 5-15/hour, 15-30/hour and ≥ 30/hour states mild, moderate and severe OSA, respectively. The majority of patients underwent preoperative P(S)G before 2012, whereas mandatory P(S)G was performed in all bariatric surgery patients, preoperatively, from 2012 onwards. CPAP was not prescribed in patients with an AHI below fifteen.

When the AHI in supine position was at least twice as high as the AHI in non-supine position, patients were considered positional. According to the Cartwright criteria, this only leads to POSA diagnosis when patients reach a total AHI above five, denoting OSA, and a supine sleeping position between 10 and 90% of TST[11]. Since mostly all bariatric patients sleep in supine position directly after surgery, these preoperative % TST are not valuable. For this reason, no limitations concerning these % TST were made for this study.

Postoperative monitoring

Patients with an AHI below fifteen received no CPAP treatment and were admitted to the general surgical ward for a 24-hour observation. Vital parameters, including blood pressure, heart rate, saturation rate and temperature were measured, intermittently. Continuous monitoring was not performed within this population.

Postoperative outcome

The primary endpoint of this study was both the cardiopulmonary complication- and mortality rate between POSA and non-POSA patients in the first 30-day postoperative period. The secondary endpoint was the evaluation of POSA predictors.

Data collection

Required data were collected from electronic medical records. Baseline variables included gender, age, body mass index (BMI), neck circumference, Mallampati score, pulmonary- and/or cardiac comorbidities, type of surgery, smoking, total AHI, AHI and % TST in supine position and sedative use. All cardiac and pulmonary complications, occurring within 30 days after bariatric surgery, were reported.

All data were anonymously entered in a database. The local ethical committee of the Director board of the hospital provided approval for this study, whereas approval of the Medical Ethical Committee (MET) was not obligated for studies within these limitations. Formal informed consent was not required for this type of study.

Statistical analysis

Baseline characteristics of POSA and non-POSA patients were documented with mean/standard deviation or median/range, when normally or not-normally distributed, respectively. Categorical variables were compared with chi-square test, whereas continuous variables were compared with the independent t-test or Mann-Whitney U test, depending on normality, which was tested with the Kolmogorov-Smirnov test.

Analysis of postoperative cardiopulmonary complications between POSA and non-POSA groups was completed with Fisher's exact test.

Predictors for POSA were evaluated through uni- and multivariable logistic regression analysis. All independent variables counting more than ten events and showing p values < 0.2 were eligible for multivariable analysis, which was achieved through backward selection. The optimal prediction model was evaluated with -2Log likelihood. Significance level for baseline variables and multivariable regression analysis was set at p value < 0.05.

RESULTS

Patient characteristics

A total of 1938 bariatric surgical procedures were performed in the period of March 2006 until October 2014. Primary LRYGB or LSG was performed in 1254 of these patients, of which 838 were excluded due to an AHI below five or above fifteen. After excluding another 139 patients due to either missing (n=108) or incomplete P(S)G data (n=28), which mainly was a result of P(S)G elsewhere, or CPAP-use despite an AHI below fifteen (n=3), a total of 277 patients, of which 153 (55%) and 124 (45%) with and without POSA, respectively, were included in this study. Comparison of baseline characteristics is displayed in Table 1, showing a significant difference in age, BMI, AHI in supine position, % of TST in supine position and pulmonary comorbidity. PG and PSG were performed in 189 (68.2%) and 88 (31.8%) patients respectively. In PG patients, the mean AHI was 8.9 (2.9), whereas in PSG patients, the mean AHI was 9.6 (2.9), p = 0.08.

A total of 136 patients had no (n=108) or incomplete (n=28) P(S)G data, resulting in exclusion from analysis. As these missing data could have an effect on current results, baseline characteristics of this group were calculated in a subanalysis. This group included 106 (78%) and 30 (22%) women and men, respectively. Mean age was 44.8 (11.1) and mean BMI 45 (6.6). LRYGB was performed in 123 (90%) patients, whereas LSG was performed in 13 (9.6) patients. A total of 46 (33.8%) patients had a history of pulmonary comorbidity, of which 20 (43.5%) had OSA on CPAP with unknown AHI. This results in missing relevant P(S)G registrations of 116 instead of 136 patients.

Postoperative complications

Of the 277 included patients, three experienced one or more postoperative cardiopulmonary complications. One of these patients experienced respiratory insufficiency and cardiac asthma, leading to reintubation and medicinal treatment. The other two patients experienced pneumonia, leading to antibiotic treatment, and sinus tachycardia, which needed no intervention. No deaths occurred. No significant difference was found between POSA and non-POSA groups (p = 0.589; OR = 0.401). Results are displayed in Table 2.

Predictors POSA

Evaluation of predictors for POSA was achieved through uni- and multivariable logistic regression analysis. All relevant baseline characteristics, including age, gender, preoperative BMI, AHI, neck circumference, Mallampati score, pulmonary- and cardiac comorbidity and smoking were analyzed. Continuous variables were checked on linearity. Since age was not linear, this variable was divided in two equal groups. Multivariable analysis was completed with variables age, gender, BMI, AHI and pulmonary comorbidity, as all these variables reached a significance level below 0.2

Table 1 - Comparison of baseline characteristics

Variables	AHI < 15 without POSA *(n = 124)*	AHI < 15 with POSA *(n = 153)*	p value
Gender (%)			NS
Female	110 (88.7)	131 (85.6)	
Male	14 (11.3)	22 (14.4)	
Age in years (SD)	45.4 (10.2)	42.9 (10.3)	0.042a
Preoperative BMI in kg/m² (range)	45.3 (41.6)	42.7 (34.5)	0.011b
Type of surgery; n (%)			NS
LRYGB	117 (94.4)	140 (91.5)	
LSG	7 (5.6)	13 (8.5)	
Total AHI (range)	9.0 (9.9)	8.3 (9.9)	NS
AHI in supine position (range)	7.3 (24.9)	15.3 (91.5)	< 0.01[b]
TST % in supine position (range)	30.1 (99.8)	40.0 (98.1)	0.023[b]
AHI in non-supine position (range)	8.5 (29.2)	3.7 (14.1)	< 0.01 [b]
Neck circumference; cm (range)	41.0 (14.0)	41.0 (18.5)	NS
Mallampati score; n (%)			NS
1	54 (50.5)	60 (51.7)	
2	35 (32.7)	38 (32.8)	
3	12 (11.2)	10 (8.6)	
4	6 (5.6)	8 (6.9)	
Pulmonary comorbidity; n (%)	34 (27.4)	26 (17.0)	0.036 [c]
Asthma	22 (17.7)	17 (11.1)	
COPD	12 (9.7)	9 (5.9)	
Pulmonary embolism	3 (2.4)	1 (0.7)	
Other[1]	2 (1.6)	3 (2.0)	
Cardiac comorbidity; n (%)	58 (46.8)	65 (42.5)	NS
Hypertension	54 (43.5)	63 (41.2)	
Myocardial infarction	1 (0.8)	3 (2.0)	
Angina pectoris	3 (2.4)	0 (0)	
Arrhythmias	5 (4.0)	5 (3.3)	
Other[2]	4 (3.2)	1 (2.0)	
Chronic sedative use; n (%)	0 (0)	0 (0)	NS
Smoking; n (%)			NS
No	73 (59.8)	91 (60.3)	
Yes	21 (17.2)	28 (18.5)	
Former	28 (23.0)	32 (21.2)	

AHI = Apnea Hypopnea Index; BMI = Body Mass Index; COPD = Chronic Obstructive Pulmonary Disease; LRYGB = Laparoscopic Roux-en-Y Gastric Bypass; LSG = Laparoscopic Sleeve Gastrectomy; SD = Standard Deviation

[1] Sarcoidosis; emphysema; mononucleosis infectiosa; non-small-cell lung carcinoma

[2] Decomensatio cordis; valve insufficiency; cardiomyopathy; pericarditis

[a] Independent t-test; [b] Mann-Whitney U test; [c] Chi-square test

Table 2 - Postoperative complications

		Complications		
		Yes	No	Total
POSAS	Yes	1	152	153
	No	2	122	124
Total		3	274	277

Fisher's Exact Test: p = 0.589
Odds Ratio = 0.401

in univariate analysis. Backward selection resulted in elimination of variables gender, AHI and pulmonary comorbidity, consecutively, resulting in a model that includes age (OR 0.464; 95% C.I. 0.282-0.764) and BMI (OR 0.946; 95% C.I. 0.909-0.984). With all five univariate significant variables, these two provided the most optimal prediction model according to the -2Log likelihood (366.4). Both uni- and multivariable logistic regression analyses are shown in Table 3 and 4.

Table 3 - Univariate logistic regression analysis; predictors for POSA

Variable	Intercept (B)	OR	95% CI	p value
Age (two equal groups)				
19-44				
45-68	-0.622	0.537	0.332-0.867	0.011
Gender				
Female				
Male	.960	2.611	1.219-5.591	0.013
BMI	-0.044	0.957	0.922-0.994	0.024
AHI	-0.062	0.940	0.866-1.020	0.137
Neck circumference	0.000	1.000	0.933-1.071	0.989
Mallampati score				
1				
2	-0.182	0.833	0.272-2.555	0.750
3	-0.205	0.814	0.257-2.581	0.727
4	-0.470	0.625	0.162-2.413	0.495
Pulmonary comorbidity	-0.668	0.513	0.228-1.154	0.107
Cardiac comorbidity	-0.079	0.924	0.510-1.674	0.794
Smoking				
No				
Yes	0.275	1.316	0.604-2.867	0.489
Former	0.335	1.397	0.536-3.644	0.494

AHI = apneu/hypopneu index; BMI = body mass index

Table 4 - Multivariable logistic regression analysis; predictors of POSA

Variable	Intercept (B)	SE	OR	95% CI	p value
Age (two equal groups)					
19-44					
45-68	-0.768	0.225	0.464	0.282-0.764	< 0.01
BMI	-0.056	0.020	0.946	0.909-0.984	< 0.01
Constant	3.122	0.958	22.680		< 0.01

BMI = Body Mass index
-2Log likelihood = 366.397
Nagelkerke R2 = 0.069

DISCUSSION

Study population

In this bariatric surgery population with mild OSA, the prevalence of POSA was 55%. Since the AHI was found to be a negative predictor for POSA, this percentage is in agreement with literature, reporting a prevalence of 34% in the overall bariatric population, including all levels of OSA severity[13].

A total of 136 patients had no (n=108) or incomplete (n=28) P(S)G data. There may be a difference in those who were excluded due to P(S)G done elsewhere, those who were excluded due to incomplete P(S)G data and those who underwent no P(S)G due to lacking symptoms. Since mild OSA is the focus of this study and the latter group is more likely to have no or mild OSA, these missing data could have an effect on current results.

Three patients were excluded from analysis as they used CPAP, despite an AHI below fifteen. Although the exact explanation for CPAP prescription in these patients was not determined, a possibility is that mild OSA diagnosis was combined with significant clinical symptoms such as daytime sleepiness.

Postoperative cardiopulmonary complications

The primary objective was to evaluate the cardiopulmonary complication rate among mild OSA patients with and without POSA, after bariatric surgery. With a limited amount of three severe complications (1.1%), no difference was found between POSA and non-POSA patients. There were no observed minor complications such as need for oxygen therapy. Except for the three patients with severe complications, no other patient had a longer length of hospital stay or higher hospital costs for cardio-pulmonary reasons. No data are available in order to compare the complication rate in OSA patients undergoing other surgery than bariatric surgery due to lacking mandatory P(S)G performance in other surgical groups.

The three complications found in study are not likely to be caused by mild OSA, as in a larger analysis, including all patients with an AHI between zero and fifteen, no difference in cardiopulmonary complication rate was found. This analysis included 651 patients, of which 277 and 374 had mild OSA and no OSA, respectively. Mean AHI of patients without OSA was 2.2 (1.5), mean AHI in supine position 4.1 (7.1) and % TST in supine position was 33.5 (24.2). No patient had POSA with a relevant supine AHI, denoting an AHI above fifteen. A total of eight postoperative cardiopulmonary complications, of which three in the OSA and five in the non-OSA group, occurred ($p = 0.768$).

Therefore, all postoperative cardiopulmonary complications of this study might have been a result of other non-pulmonary conditions than OSA. This concludes that in terms of severe cardiopulmonary outcome, CPAP therapy is not indicated in patients with mild OSA undergoing bariatric surgery, despite being positional. However, this retrospective analysis has shown that cardiopulmonary events and deaths are

relatively rare in both POSA and non-POSA patients. Therefore, in order to detect significant differences between both groups, larger studies are needed.

Moreover, postoperative %TST was not evaluated. While it is thought that many patients sleep in supine position for surgical safety reasons after surgery, this was not objectified. This might have introduced bias to the study. Preoperative P(S)G showed that 37 (13.4%) patients had < 10% TST in supine position and 11 (4%) patients had < 10% TST in non-supine position. Since the Cartwright criteria for POSA diagnosis include supine sleeping position between ten and 90% of TST, these patients may have had an ambiguous definition of OSA. In addition, patients who underwent PG may have a reported AHI that underestimates the true AHI.

New forms of positional therapy (PT) with smart vibrating devices worn on the chest, that prevent patients from sleeping on the back, without negatively influencing sleep quality, are rapidly gaining attention[15-17]. PT might be reserved for POSA patients experiencing desaturations and/or clinical symptoms. Both were not observed in this study. PT might also be considered in patients with an AHI > 15/hour, who are positional and cannot accept CPAP. Since a significant excess weight loss (59-66%[18-19]) is expected after surgery, the AHI decreases likewise[13]. Here severe non-positional OSA might reverse into less severe positional OSA. Taken this in mind, medical professionals must always evaluate patients' individual symptoms, providing an opportunity for therapy.

Predictive factors POSA

Evaluation of predictive factors for POSA was achieved through multivariable logistic regression analysis, revealing variables age and BMI as negative predictors. Although this is in agreement with the literature[20-21], little variance is explained for the POSA prediction model with these two variables (Nagelkerke R2 = 0.069). This implies that the majority is explained by variables not included in this analysis. Although earlier studies reported the AHI as negative predictor for POSA[12-13;20-22], this was not found in the current study. Additionally, neck circumference appeared no predictor in current analysis, whereas contrasting results were published by Mador et al. and Teerapraipuk et al.[12;22]. Although five univariate variables reached a significance level below 0.2 in this study, only two were significant in multivariable analysis. This suggests that other settings and larger sample sizes might provide a better prediction model.

CONCLUSION

After bariatric surgery, only 1.1 % of patients with mild OSA experienced severe cardiopulmonary complications. No difference was found between POSA and non-POSA patients. These results conclude that in terms of 30-day postoperative cardiopulmonary outcome, mild OSA patients undergoing bariatric surgery do not require CPAP therapy, despite being positional in more than 50 % of cases. However, positional therapy might be considered in mild POSA patients who experience substantial clinical symptoms, and in patients with more severe OSA, who are positional and cannot accept CPAP. In multivariable analysis, age and BMI were found to be significant negative predictors for POSA.

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Influence of continuous positive airway pressure on postoperative leakage in bariatric surgery

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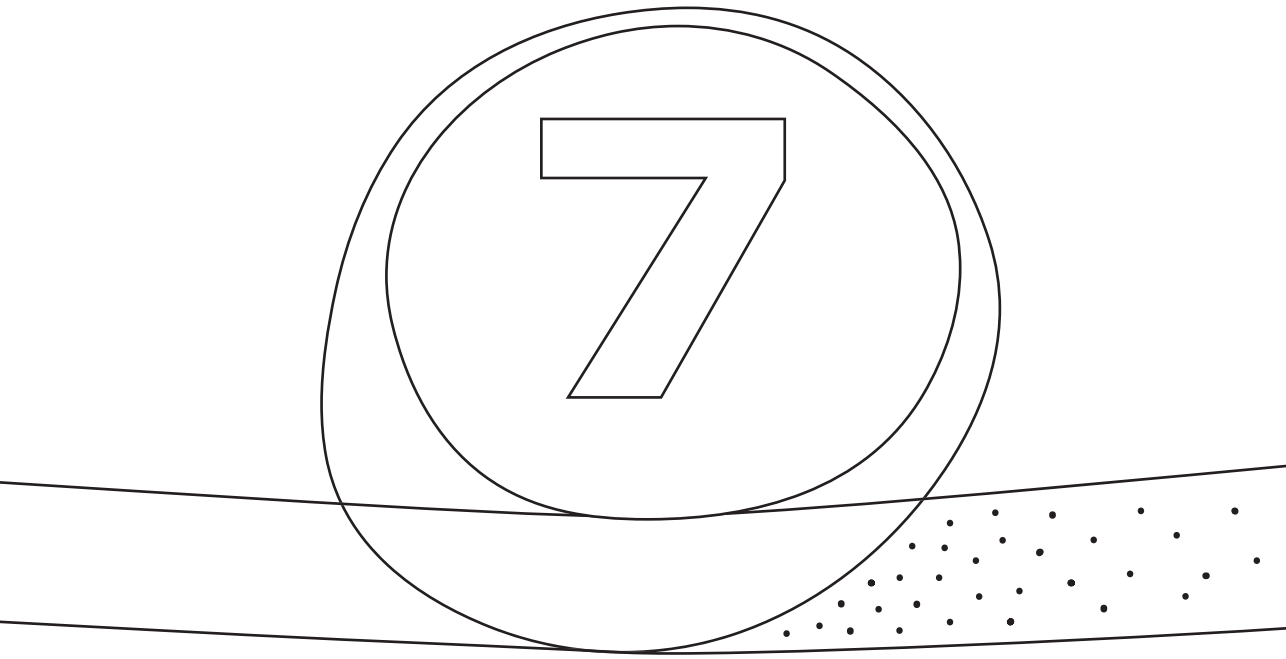

ABSTRACT

Introduction: Obstructive sleep apnea (OSA) affects two-third of morbidly obese individuals undergoing bariatric surgery. Perioperative usage of continuous positive airway pressure (CPAP) is advised for moderately and severe OSA to avoid respiratory failure and cardiac events. CPAP increases the air pressure in the upper airway, but also may elevate the air pressure in the esophagus and stomach. Concern exists that this predisposes to mechanical stress resulting in suture or staple line disruption (further referred to as suture line disruption).

Objectives: To evaluate whether perioperative CPAP usage is associated with an increased risk of suture line disruption after bariatric surgery.

Setting: Obesity Center Amsterdam, OLVG-west, Amsterdam, the Netherlands.

Methods: All patients who underwent bariatric surgery including a suture line were eligible for inclusion. Only patients with information regarding OSA severity as defined by the apnea-hypopnea-index (AHI) and postoperative CPAP usage were included.

Results: From November 2007 to August 2016, postoperative CPAP status was documented in 2135 patients: 497 (23.3%) used CPAP postoperatively whereas 1638 (76.7%) used no CPAP. Mean body mass index was 44.1 kg/m^2 (SD 6.6). Suture line disruption occurred in 25 patients (1.2%). The leakage rate was not associated with CPAP usage (8 (1.6%) in CPAP group versus 17 (1%) in non-CPAP group, p=0.300). CPAP was no risk factor for suture line disruption in multivariable analysis as well.

Conclusion: Postoperative CPAP does not appear to increase the risk of suture line disruption in bariatric surgery. CPAP is recommended in all patients with moderate or severe OSA who undergo bariatric surgery.

INTRODUCTION

Excessive adipose tissue, obesity, affects cardiovascular function, glucose metabolism and musculoskeletal performance. The overall global population is progressively affected by obesity. Worldwide, the prevalence increased from 5-8% in 1980 to 13% in 2014[1]. Except for parts of sub-Saharan Africa and Asia, all regions include more individuals with obesity than underweight[1]. Morbidity due to obesity can be reversed by diets, physical exercise or bariatric surgery. The latter modality is reserved for those individuals with morbid obesity, which represents such severe forms of obesity that prevent normal physical activity and cause onset of pathologic conditions. Defining morbid obesity remains a difficult task as obesity related health risks vary among individuals. Commonly used definitions are a body mass index (BMI) greater than 40 kg/m^2 and a BMI greater than 35 kg/m^2 with coexistence of obesity related comorbidities. In 2013, over 500,000 bariatric surgical procedures were performed worldwide[2].

One-third of the morbidly obese population has a moderate or severe form of obstructive sleep apnea (OSA), a disease that is characterized by at least 15 events of obstruction of the upper airway per hour during sleep[3]. OSA is associated with an increased risk of postoperative respiratory failure and cardiac events[4]. The Society of Anesthesia and Sleep Medicine guidelines recommend the perioperative usage of continuous positive airway pressure (CPAP) therapy to reduce this risk[5].

CPAP provides continuous pressure in the upper airway which is directly connected to the upper gastro-intestinal tract, and concern exists that the increased intraluminal pressure in the esophagus and stomach predisposes to mechanical stress resulting in suture or staple line disruption (further referred to as suture line disruption). The prevalence of suture line disruption is 1.9% after laparoscopic Roux-en-Y gastric bypass (LRYGB) and 2.3% after laparoscopic sleeve gastrectomy (LSG)[6]. Leak associated mortality varies between 6.3% and 16.7%[7-9].

The influence of postoperative CPAP usage on suture line disruption was evaluated in three studies, which all concluded that CPAP was not associated with an increased leakage rate[10-12]. Ramirez and colleagues reported the largest sample size of 310 patients and stated that a larger series would be necessary to assess the differences between groups[10]. This study presents an analysis of more than 2000 patients.

METHODS

Study design and population

All patients who underwent bariatric surgery at the Obesity Center Amsterdam, the Netherlands, met the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) criteria for bariatric surgery. All surgical procedures including a suture line were eligible for inclusion. Those with available data on CPAP usage were finally included. Data were retrospectively collected from patient medical records and registered in an anonymous database. The Institutional Review Board provided approval for this study. Obtaining informed consent for this study was not required.

Surgical procedures

All bariatric procedures including a suture line were considered for inclusion. These included Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG), one anastomosis gastric bypass (OAGB) and single anastomosis duodeno-ileal bypass with sleeve gastrectomy (SADI-S). Both primary and revisional procedures were included. All surgical procedures were performed laparoscopically and according to standardized techniques. Anastomoses were created with linear Echelon Flex™ (Johnson and Johnson, Somerville, NY, USA) and V-lock™ (Covidien, Dublin, Ireland). Staple lines were created with above mentioned staplers. The Seamguard Reinforcement™ (Gore, Newark, Delaware, USA) was introduced for SG procedures in May 2016 and has been used on routine basis few months later.

OSA and CPAP

From 2012 onwards, all patients scheduled for bariatric surgery undergo a poly(somno) graphy (P(S)G) to evaluate the presence of OSA and its severity. Prior to this period, sleep studies were only performed in limited cases. Reasons for performing these sleep studies were severe complaints that may be related to OSA or high clinical suspicion by the physician. Some patients had undergone a sleep study prior to referral to a bariatric clinic. The apnea-hypopnea-index (AHI) is a severity index for OSA and represents the number of apneic events per hour during sleep. An AHI greater than 15/hour defines moderate or severe OSA and is generally an indication for CPAP therapy. Indicating need for CPAP therapy is a collaboration of the otorhinolaryngologist and pulmonologist. The amount of positive pressure is variable. Patients are asked to bring their own CPAP mask and machine to the hospital.

Statistical analysis

All data were analyzed using SPSS 21.0 for Windows (SPSS Inc. Chicago Illinois, USA). Continuous baseline variables were compared with independent t-test or Mann-Whitney U test, depending on normality evaluated with histograms. Categorical variables were compared with Chi-square test. Effect of CPAP usage on leakage rate was calculated with Chi-square test. The predictive value of CPAP usage and CPAP pressure for suture line disruption was evaluated with (multivariable) logistic regression analysis.

RESULTS

Study population

From November 2007 until August 2016, 2410 patients underwent a bariatric procedure including a suture line. Information regarding postoperative CPAP usage was available in 2135 (88.6%) patients. Of these patients, 1747 (81.8%) were female and 388 (18.2%) male. Mean BMI was 44.1 kg/m^2 (SD 6.6), mean age 44.3 years (SD 11.2) and median AHI 7.1/hour (0-151). Of 2135 included patients, 497 (23.3%) used CPAP in the direct postoperative period. The majority (n=1609; 75.4%) underwent primary RYGB. Other performed procedures included primary SG (n=153; 7.2%), SADI-S (n=2; 0.09%), OAGB (n=2; 0.09%), conversion from adjustable gastric banding (AGB) to RYGB (n=318; 14.9%), conversion from AGB to SG (n=28; 1.3%), conversion from SG to RYGB (n=16; 0.7%), VBG to RYGB (n=4; 0.19%) and VBG to SG (n=3; 0.1%).

Suture line disruption/postoperative leakage

Suture line disruption occurred in 25 (1.2%) patients after bariatric surgery. Patients in the leakage group were significantly older, and more patients had hypertension. Baseline characteristics of patients with and without leakage are shown in Table 1. Leakage associated mortality was 12% (3 of 25 patients).

Table 1 - Baseline variables between patients with and without suture line disruption

Variable	Leakage: no (n=2110)	Leakage: yes (n=25)	p-value
Gender			0.777[1]
Female (%)	1726 (81.8)	21 (84.0)	
Male (%)	384 (18.2)	4 (16.0)	
Age (SD); years	44.3 (11.2)	47.8 (8.3)	0.044[2]
BMI (SD); kg/m^2	44.1 (6.5)	45.7 (9.8)	0.219[2]
Waist circumference (SD); cm	128.5 (14.7)	137.9 (21.4)	0.054[2]
Primary surgery (%)	1748 (82.8)	19 (76.0)	0.368[1]
Revisional surgery (%)	362 (17.2)	6 (24.0)	
AHI (range)	7 (0-151)	12.6 (0.4-149)	0.096[3]
AHI in supine position (range)	8.1 (0-198)	9 (0-160)	0.453[3]
CPAP usage postoperative (%)	489 (23.2)	8 (32.0)	0.299[1]
Hypertension (%)	792 (37.5)	16 (64.0)	0.007[1]
Type II diabetes (%)	532 (25.2)	9 (36.0)	0.218[1]
Dyslipidemia (%)	385 (20.7)	7 (33.3)	0.157[1]

[1] = Chi-square; [2] = independent t-test; [3] = Mann-Whitney U test

AHI = Apnea Hypopnea Index; BMI = Body Mass Index; CPAP = Continuous Positive Airway Pressure; SD = Standard Deviation

Influence of CPAP

Suture line disruption occurred in 8 out of 497 (1.6%) patients who used CPAP in the postoperative period and in 17 out of 1638 (1%) patients without postoperative CPAP usage. There was no difference between groups (p = 0.03).

Median perioperative CPAP pressure was 8 mmHg (IQR 7.2-9.6; n=120); median maximal pressure 13 mmHg (IQR 10-14; n=328) and median AHI with CPAP 2 events/hour (IQR 2-4; n=327). These variables had no influence on suture line disruption. Results of CPAP pressures between patients with and without leakage are shown in Table 2.

Table 2 - CPAP pressures between patients with and without suture line disruption

Variable	Leakage: no (n=489)	Leakage: yes (n=8)	p-value
Postoperative CPAP usage (%)	489 (23.2)	8 (32)	0.299[1]
Median CPAP pressure (range)	8 (4.2-13) *n=118*	9.1 (6.7-11.5) *n=2*	0.910[2]
Median maximal CPAP pressure (range)	13.3 (6-18) *n=320*	13 (10-14) *n=8*	0.850[2]
Median AHI with CPAP (range)	2 (0-45) *n=323*	2 (1.1-4.4) *n=4*	0.992[2]

[1] = Chi-square; [2] = Mann-Whitney U test

AHI = Apnea Hypopnea Index; CPAP = Continuous Positive Airway Pressure

Predictive factors of suture line disruption/postoperative leakage

Postoperative CPAP usage was not an independent predictor for postoperative suture line disruption (OR 1.56; p=0.303). Continuous variables age and waist circumference showed no linearity with leakage resulting in both variables to be divided in two equal groups. Age (cut-off 45 years) was not an independent predictive factor (OR 1.96, 95% CI 0.863-4.460, p=0.108). Only waist circumference (cut-off 128 cm; OR 2.47, 95% CI 1.026-5.930, p=0.044) and hypertension (OR 2.96, 95% CI 1.301-6.727, p=0.010) were significant univariable predictors for leakage. In multivariable analysis, hypertension remained a strong predictor (OR 2.817, 95% CI 1.247-6.417, p=0.014), whereas waist circumference appeared a less strong predictor (OR 2.315, 95% 0.961-5.578, p=0.061).

DISCUSSION

Suture line disruption after bariatric surgery occurred in 1.2% and was associated with a mortality rate of 12%. These percentages are similar to previous studies[7-9]. The current study shows that postoperative CPAP usage is not associated with an increased leakage rate. Results were in accordance with Ramirez et al. who reviewed 310 LRYGB patients of which 219 (70.7%) used CPAP in the immediate postoperative period. No anastomotic leakages occurred in either group. The incidences of atelectasis, gastrointestinal bleeding and wound infection were not different different between patients with and without CPAP usage.

Current sample size (n=2135) is large enough to detect a difference of 1.05%. As this is clinically acceptable, postoperative CPAP usage can be safely recommended. Obviously collecting more data would be valuable to further reduce this percentage.

Literature regarding the effect of CPAP on the intraluminal pressure is scarce, but one small study investigated the effect of CPAP on the transmural pouch pressure in 28 patients after RYGB. Pressures were measured prior to initiation of CPAP during post anesthesia care unit (PACU) arrival, 5 and 30 minutes after CPAP usage and prior to PACU discharge. Pouch pressures were not different between time moments, thereby implying that CPAP usage after RYGB does not pose a risk for pouch distension and hence does not increase the risk for suture line disruption[13].

The influence of CPAP usage on other than bariatric related suture lines was investigated in one other study which described the effect of CPAP directly after extubation in congenital tracheoesophageal fistula and esophageal atresia. No leakages occurred in the CPAP group (n=10), whereas 4 out of 41 patients in the non-CPAP group developed leakage, p=0.57[14]. Existing literature suggests CPAP usage to be safe in all types of esophageal and upper abdominal surgery. Patients with malignant diseases might be a different group as these patients have overall decreased health and hence increased risk of suture line disruption after esophageal or gastric surgery for malignancies.

Hypertension was the strongest predictor for anastomotic leakage in this study. This is explained by its negative effect on the microvasculature supplying the anastomosis. Also in other surgery groups, hypertension has shown to be an independent risk factor for anastomotic leakage[15-17]. In a recent report of Tao et al. hypertension was no predictor for mortality in obesity surgery[18].

In conclusion, postoperative CPAP usage does not appear to increase the risk of suture line disruption in bariatric surgery and can therefore be safely recommended.

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Do complications alter postoperative weight loss one year after primary and revisional Roux-en-Y gastric bypass?

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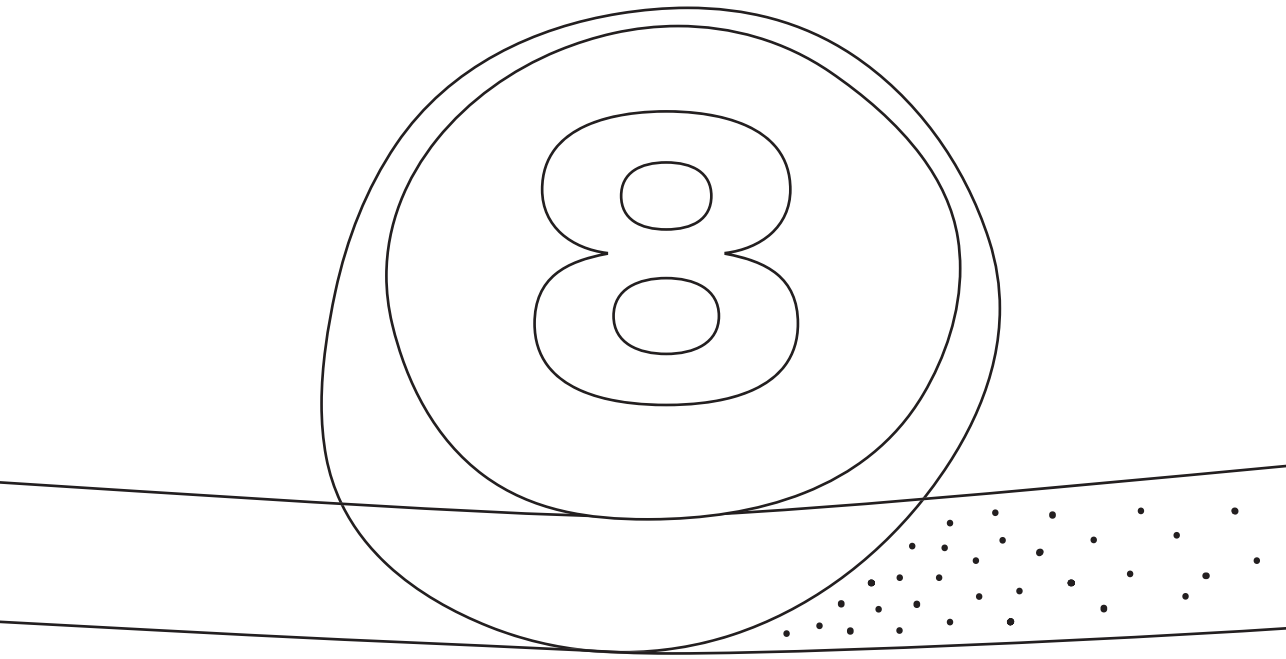

ABSTRACT

Introduction: Around 10% of bariatric surgery patients experience postoperative complications (<30 days). It could be hypothesized that complications influence postoperative weight loss, which is one of the most important endpoints of bariatric surgery. Therefore, this study inventoried the effect of complications on postoperative weight loss.

Methods*:* A consecutive database including patients who were operated from November 2007 onwards was retrospectively reviewed. All short-term complications were classified according to the Clavien-Dindo classification. Weight loss was assessed at six and 12 months postoperatively.

Results: A total of 1130 patients underwent either primary (n=907, 80.3%) or revisional (n=233, 19.7%) surgery till October 2013. Short-term complications occurred in 115 (10.2%) patients, of whom 48 (41.7%) had a severe (Clavien-Dindo ≥ 3) complication. One year post surgery, 184 patients (16.3%) were lost to follow-up. Patients with a short-term complication had higher percentage excess weight loss (%EWL) at six months (58.6 SD 16.6 versus 52.9 SD 17.6, $p < 0.01$) and one year (71.9 SD 22.3 versus 65.9 SD 21.3, p=0.017) follow-up. Although a trend was seen towards higher BMI loss and total weight loss (TWL) after six months, no effect was seen one year postoperatively. In multivariable linear regression analysis, complications were no significant predictor for one year %EWL.

Conclusion: Although short term complications alter one year %EWL, no effect was seen on BMI loss and TWL. In addition, complications were no predictor in a multivariable linear regression model for one year %EWL. It can be concluded that short-term complications do not impair weight loss after Roux-en-Y gastric bypass.

INTRODUCTION

Obesity and morbid obesity are a growing health problem with more than 600 million obese people worldwide. The only long term effective solution for morbid obesity (Body Mass Index (BMI) above 40 kg/m^2 or BMI above 35 kg/m^2 with one or more obesity related comorbidities) is bariatric surgery[1]. Since the introduction of laparoscopic surgery, the number of bariatric surgical procedures rapidly increased[2]. The majority of these procedures include the laparoscopic Roux-en-Y gastric bypass (LRYGB) (47%) and laparoscopic sleeve gastrectomy (LSG) (28%)[3]. Although bariatric surgery is considered relatively safe, around 4.3-14.5% of the patients undergoing primary surgery develop an early (≤ 30 day) postoperative complication[4;5]. Severe complications are seen in 3.4-4.3% of the patients[6;7]. As the laparoscopic adjustable gastric band (LAGB) has a high rate of adverse events in the long term, numerous patients opt for revisional surgery into LRYGB or LSG[8-10]. However, this revisional surgery has a higher complication rate compared to primary procedures[8].

Although some of these complications require re-interventions and long-term hospitalization, mortality due to bariatric surgery is only 0.2%.

However, the effect of short term (including severe) complications on postoperative outcomes has not clearly been investigated yet. In the long term, weight loss is one of the most important endpoints of bariatric surgery. Complications, especially severe ones, could have an influence on the postoperative weight loss. As patients with a severe complication, such as anastomotic leakage, often require interventions and/or prolonged Intensive Care Unit (ICU) admission without the possibility of enteral nutrition, this could influence the postoperative weight loss. Furthermore, critically ill patients need a higher number of calories and proteins for recovery, but on the contrary, once home, often lack the energy to increase their activities and exercise. Many patients at the ICU, suffer from critical illness polyneuropathy which may not fully recover after discharge, causing difficulties in the daily life[11]. It could be hypothesized that patients with a short-term complication will lose more weight at 6 and 12 months follow-up than patients without a short-term complication. If confirmed, findings would support targeted follow-up, increased awareness and support of this population in the early post-operative period. Whether postoperative weight loss is influenced by the early postoperative period is therefore an important clinical topic of interest.

Therefore, the aim of this study was to inventory the influence of short-term complications on postoperative weight loss, six months and one year after surgery.

METHODS

A retrospective analysis was performed with a computerized prospective database including all consecutive patients undergoing bariatric surgery from November 2007 onwards. Eligible for inclusion were patients who underwent either primary or revisional LRYGB from November 2007 till October 2013. At least six months follow up were required for final inclusion. As the sample size of patients who underwent LSG is small and in order to avoid bias of study results, LSG patients were excluded. In addition, patients with perioperative cancellation of the procedure due to any reason were excluded. All patients met the IFSO criteria prior to surgery[12].

Preoperative screening

All patients scheduled for bariatric surgery were preoperatively screened by a specialized multidisciplinary team. This screening existed of physical, psychological and dietary evaluation.

In addition to this standardized screening, all patients were submitted to esophagogastroduodenoscopy to detect lesions in the future remnant stomach. From 2012 onwards, all patients underwent mandatory poly(somno)graphy as diagnostics for obstructive sleep apnoea (OSA). The severity of OSA was based on the apnea-hypopnea-index (AHI): an AHI of 0-5/hour is no OSA, 5-15/hour mild OSA, 15-30/hour moderate OSA and above 30/hour severe OSA.

Preoperatively, patients were counselled to stop smoking and non-steroidal anti-inflammatory drugs were stopped.

Surgical procedure

LRYGB was performed by three experienced bariatric surgeons or under their direct supervision according to a standardized protocol as previously described[13].

In all patients, the proximal jejunal part was identified and the future location of the gastrojejunostomy (GJ) was tested to assess whether a tension free anastomosis was technically feasible. The pouch of approximately 30 ml was created in the lesser curvature and subsequently the Roux limb was positioned in an antecolic, antegastric fashion; furthermore, both anastomosis, the GJ and jejunojejunostomy, were stapled and handsewn using a V-loc™ (Covidien, Dublin, Ireland).

In case of a revisional procedure of a previous adjustable gastric band, the surgery began with removal of the band followed by direct revision. Prior to closure of the skin the port-a-cath was removed at the end of the procedure.

Postoperative care

At the start of this cohort, patients were admitted to the general surgical ward for at least 48 hours postoperatively. Midway through the data acquisition, protocols for length of stay changed from 48 to 24 hours.

In case of moderate or severe OSA (AHI ≥ 15/hour), continuous positive airway pressure (CPAP) therapy was preoperatively prescribed and used during the perioperative period. Patients with a severe form of OSA, defined as AHI above 30, were admitted to the ICU for continuous monitoring during the first postoperative night. All other patients were admitted to the general surgical ward.

Starting in august 2011, all patients received a six months course of prophylactic pantoprazole 40 mg. Special vitamins and micronutrients were advised from the beginning.

Early postoperative complications (< 30 days)

Overall short-term complications included both surgical (e.g. anastomotic leakage, postoperative bleeding, bowel perforation) and non-surgical complication such as pneumonia, pain without an evident cause, nausea and vomiting. All the perioperative and early postoperative complications were graded according to the Clavien- Dindo classification for postoperative complications[13]. This classification system scales the severity of adverse outcomes based on the intervention needed to treat the complication and consists of five grades and two subgrades[14]. Grade I complications require no medical or surgical intervention, grade II complications need pharmacological treatment but no active intervention, grade III complications comprehend radiological/endoscopic (IIIa) or surgical (IIIb) interventions. Grade IV complications represent the life-threatening ones and are classified as grade IVa, single organ failure, and grade IVb, multi-organ failure. Finally, grade V complications are those leading to death.

Patients who had more than one adverse event were classified according to the highest grade.

Postoperative course (weight loss)

The postoperative course was evaluated with the amount of weight loss during follow up. Weight loss was defined as the percentage of excess weight loss (%EWL), which was calculated with the pre- and postoperative BMI. A BMI of 25kg/m^2 was used as an assumption of ideal weight. The formula to calculate %EWL was as follows: 100 – ((Postoperative EW / Preoperative EW) * 100). Additionally, points of BMI loss and the loss of total weight (TWL) in kilograms were analysed.

Complications occurring after 30 days were analysed as late postoperative complications.

Data collection and statistical analysis

The required data were collected from electronic patient medical records. Baseline characteristics included gender, age, preoperative BMI, waist circumference, revisional surgery, comorbidities such as OSA, type II diabetes, hypertension, dyslipidaemia and depression, and finally intoxications including alcohol and smoking. Follow-up was registered.

All data were analysed using SPSS 21.0 for Windows. (SPSS Inc. Chicago Illinois, USA). Comparison of baseline characteristics and weight loss was achieved between patients with and without overall short-term complications. Next to this, comparison was achieved between patients with Clavien-Dindo 1-2, 3a-3b and 4a-4b complications. Additionally, a subanalysis was performed only with patients who underwent primary LRYGB, whereafter weight loss was also compared between patients who underwent primary and revisional LRYGB. For the continuous variables, normal distribution was evaluated using histograms and the Kolmogorov Smirnov test. The students t-test was used to determine any statistical significance for the continue variables, the Chi-square test for the dichotomous. In addition, the One-way ANOVA with correction for multiple testing (Bonferroni) was used to compare weight loss with the severity of complications divided in three categories. Levene's test was used to assess the homogeneity of variances between groups. A 2- sided p-value of less than 0.05 was considered statistical significant. A multivariable linear regression analysis was performed in order to evaluate the predictive value of short-term complications on one year %EWL, adjusted for other factors. Additional to short-term complications, variables that predicted insufficient weight loss previously were included in the model[14]. These comprise: gender, age, BMI, waist circumference, revisional surgery, AHI and type II diabetes. As de continuous variables were not linear with the outcome, we dichotomized these variables. Age and waist circumference were divided in two equal groups, BMI was divided in BMI < 50 or ≥ 50 (super-obesity) and AHI was divided in no/mild (< 15) or moderate/severe OSA (≥ 15).

RESULTS

Study population

Primary or revisional LRYGB was performed in 1142 patients between November 2007 and October 2013.

Perioperative cancellation of the procedure was necessary in nine patients for safety reasons: in four patients severe adhesions from previous surgery impaired sight; one patient suffered from iatrogenic bleeding from the arteria gastrica sinistra; in two patients the future pouch would have been to fragile due to damage of the removed band, one patient had a dilated stomach due to the gastric band, creating difficulties for the future pouch, the last patient suffered from iatrogenic colon perforation at the ileotransversostomy from previous hemicolectomy for carcinoma, resulting in abandoning of the bariatric procedure. These nine patients were excluded from analysis, as were three patients who died (0.2%) (Clavien- Dindo 5). One patient died of an iatrogenic cardiac tamponade during removal of the band, one patient suffered from bowel necrosis after anastomotic leakage and sepsis and the other patient died of a pulmonary embolism. Consequently, a total of 1130 patients were analysed in this study.

A total of 930 (82.3%) were female, the mean age was 44 (SD 10.6) and the mean BMI 44.6 (SD 6.4). Within this group, 907 (80.3%) underwent a primary LRYGB, whereas 223 (19.7%) underwent a revisional LRYGB, mostly from (L)AGB into LRYGB (94.2%).

Postoperative complications

Overall, complications within 30 days occurred in 115 patients (10.2%), of which 64 (55.7%) had a surgical cause. Forty-four (38.3%) of these 115 patients had a complication requiring at least radiological intervention (Clavien-Dindo $\geq$ 3), being 3.9% of the entire study group. The distribution of patients according to the Clavien-Dindo system was 71 patients (61.7%) within class 1-2, 40 (34.8%) in class 3a-3b and four (3.5%) in class 4a-4b. Table 1 displays all baselines comparing patients with and without an early short term and between Clavien-Dindo classifications. None of the baseline characteristics predisposed for any of the complications.

Weight loss

Of the patients without a short-term complication, data on weight loss were available of 874 and 854 patients at six months and one year follow up respectively. Lost to follow up was 16.3% one year after surgery. These data were compared with weight loss in patients who suffered complications and were available in 93 and 92 patients after six months and one year correspondingly. Their Clavien-Dindo classification was class I-2 in 58, class 3a-3b in 31 and class 4a-4b in four patients at six months and in 56, 32 and four patients at one year, respectively.

Table 1 - Comparison of baseline characteristics – Postoperative course (< 30 days)

Variables	All patients (n = 1130)	No complication (n =1015)	Short term complications (n =115)	p-value	Clavien-Dindo 1-2 (n = 71)	Clavien-Dindo 3a-3b (n = 40)	Clavien-Dindo 4a-4b (n = 4)	p-value
Gender n (%)				0.727†				0.779†
Female	930 (82.3)	834 (82.2)	96 (83.5)		58 (81.7)	34 (85)	3 (75)	
Male	200 (17.7)	181 (17.8)	19 (16.5)		13 (18.3)	6 (15)	1 (25)	
Age in years (SD)	44.1 (10.6)	44.1 (10.6)	44.4 (10.8)	0.782‡	44.6 (11.3)	43.7 (10.2)	47.3 (6.1)	0.900*
Preoperative BMI in kg/m² (SD)	44.6 (6.4)	44.7 (6.5)	43.9 (6.1)	0.180‡	4.7 (5.6)	44.1 (7)	45.4 (7.5)	0.586*
Waist circumference in cm SD (n = 836)	130.3 (15.1)	130.3 (15.1)	130.6 (15.6)	0.872‡	128.8 (15.2)	132.9 (16.2)	137.3 (17.7)	0.543*
Type of LRYGB				0.287†				0.222†
Primary (%)	907 (80.3)	819 (80.7)	88 (76.5)		58 (81.7)	27 (67.5)	3 (75)	
Revisional (%)	223 (19.7)	196 (19.3)	27 (23.5)		13 (18.3)	13 (32.5)	1 (25)	
AHI (IQR) (n=1002)	7.3 (18.8)	7.3 (18.8)	8.7 (18)	0.327‡	9.9 (18.8)	8.7 (18.3)	4.2 (-)	0.673*
OSA severity				0.454†				0.451†
AHI 0-5 (%)	409 (40.8)	369 (40.9)	40 (40.4)		27 (42.9)	11 (33.3)	2 (66.7)	
AHI 5-15 (%)	256 (25.5)	232 (25.7)	24 (24.2)		11 (17.5)	12 (36.4)	1 (33.3)	
AHI 15-30 (%)	161 (16.1)	140 (15.5)	21 (21.2)		14 (22.2)	7 (21.2)	-	
AHI > 30 (%)	176 (17.6)	162 (17.9)	14 (14.1)		11 (17.5)	3 (9.1)	-	
NIDDM (%)	186 (16.6)	166 (16.4)	20 (17.4)	0.780†	9 (12.7)	10 (25)	1 (25)	0.380†
IDDM (%)	144 (12.7)	131 (12.9)	13 (11.3)	0.623†	8 (11.3)	5 (12.5)	-	0.861†
Hypertension (%)	468 (41.4)	416 (41)	52 (45.2)	0.383†	35 (49.3)	16 (40)	1 (25)	0.499†
Dyslipidemia (%)	290 (25.7)	259 (25.5)	31 (27)	0.707†	21 (29.6)	9 (22.5)	1 (25)	0.871†
Depression (%)	183 (16.2)	158 (15.6)	25 (21.7)	0.089†	17 (23.9)	8 (20)	-	0.200†
Alcohol (%)	440 (38.9)	390 (38.4)	50 (43.5)	0.288†	30 (42.3)	18 (45)	2 (50)	0.736†
Smoking (%)	215 (19)	191 (18.8)	24 (20.9)	0.873†	16 (22.5)	8 (20)	2 (50)	0.722†

AHI = Apnea-Hypopnea-Index; BMI = Body Mass Index; LAGB = Laparoscopic Adjustable Gastric Banding; LRYGB = Laparoscopic Roux-en-Y Gastric Bypass; LSG = Laparoscopic Sleeve Gastrectomy; SD = Standard Deviation; †Chi square; ‡ Independent sample T-test; * One-Way ANOVA

Table 2 - Complications and weight loss

Postoperative outcome	All patients	No complication	Short term complication	p-value†	Clavien-Dindo 1-2	Clavien- Dindo 3a-3b	Clavien- Dindo 4a-4b	p-value*
BMI (kg/m2) loss 6 months n=967 (SD)	10.9 (3.3)	10 (3.3)	10.6 (2.9)	0.080	10.6 (2.8)	10.5 (3)	11.7 (2.3)	0.392
BMI (kg/m2) loss 1 year n=946 (SD)	12.7 (4.3)	12.5 (4.3)	13.2 (3.9)	0.122	13.1 (3.9)	13.4 (4.1)	13 (3.2)	0.533
%EWL 6 months n=967 (SD)	53.4 (17.6)	52.9 (17.6)	58.4 (16.6)	0.003	58.5 (16.3)	58 (18)	60.8 (15.3)	0.039[1]
%EWL 1 year n=946 (SD)	66.5 (21.5)	65.9 (21.3)	71.9 (22.3)	0.017	71.5 (22.7)	73.2 (22.7)	66.6 (14.5)	0.083
TWL (kg) 6 months n=967 (SD)	28.9 (10)	28.7 (10.1)	30.5 (8.9)	0.074	29.9 (8.5)	30.9 (10)	34.5 (7.5)	0.326
TWL (kg) 1 year n=946 (SD)	36.1 (13.2)	35.9 (13.2)	37.7 (12.2)	0.180	37.1 (12.3)	38.8 (12.4)	38.3 (10.3)	0.588

BMI = Body Mass Index; EWL = Excess Weight Loss; SD = Standard Deviation; TWL = Total Weight Loss

† *T-test;* ** One way ANOVA*

[1] After correction for multiple testing (Bonferroni): no significant difference

Table 3 - Subanalysis: primary bariatric surgery

Postoperative outcome	All patients (n = 907)	No complication	Short term complication	p-value†	Clavien-Dindo 1-2	Clavien- Dindo 3a-3b	Clavien-Dindo 4a-4b	p-value*
BMI (kg/m^2) loss 6 months n=788 (SD)	10.6 (3.1)	10.6 (3.1)	11 (2.6)	0.232	10.9 (2.5)	11.3 (3)	10.8 (1.9)	0.697
BMI (kg/m^2) loss 1 year n=771 (SD)	13.4 (4)	13.3 (4)	13.8 (3.5)	0.321	13.6 (3.4)	14.6 (3.8)	11.5 (1.6)	0.413
%EWL 6 months n=788 (SD)	54.6 (16.8)	54.1 (16.7)	59.6 (16.4)	0.008	60.1 (16.1)	57.4 (17.8)	65.3 (15.1)	0.049[1]
%EWL 1 year n=771 (SD)	68.4 (20.2)	67.9 (19.9)	73.8 (21.8)	0.018	74.5 (22.5)	72.6 (21.7)	69.8 (15.9)	0.120
TWL (kg) 6 months n=788 (SD)	30.5 (9.6)	30.4 (9.7)	31.7 (8.5)	0.265	30.9 (8)	33.7 (9.9)	31.6 (6)	0.484
TWL (kg) 1 year n=771 (SD)	38.4 (12.5)	38.3 (12.6)	39.6 (11.8)	0.413	38.8 (11.6)	42.1 (12.7)	33.7 (5.7)	0.500

BMI = Body Mass Index; EWL = Excess Weight Loss; SD = Standard Deviation; TWL = Total Weight Loss

† *T-test; * One way ANOVA*

[1] After correction for multiple testing (Bonferroni): no significant difference

The mean BMI loss of the overall study population was 10.9 kg/m^2 (SD 3.3) after six months of follow up. One year after surgery, this loss increased to a mean BMI loss of 12.7 (SD 4.3) ($p < 0.001$). No significant difference was seen between patients with and without a short-term complication, or between Clavien-Dindo severity classifications.

In addition to BMI loss, mean %EWL was 53.4% (SD 17.6) after six months of surgery with a significant difference between patients with- and without a short-term complication (58.4% versus 52.9% respectively; 0.003). After one year, patients with a short-term complication still had a significant higher %EWL (71.9% versus 65.9%; $p = 0.017$). After correction for multiple testing, no significant difference in %EWL was seen between Clavien-Dindo groups at both follow-up moments.

Finally, TWL was evaluated. After six months, TWL was 28.9 (SD10) kilograms. This significantly increased to 36.1 (SD 13.2) kilograms one year after surgery. No significant difference regarding TWL detected between patients with- and without a complication, nor between Clavien-Dindo severity groups at both follow-up moments. The results are shown in **Table 2.**

Dividing the complications in Clavien-Dindo < 3 or ≥ 3, no effect was seen on BMI loss, %EWL or TWL after six months and 12 months postoperatively.

Analysis of primary LRYGB

A subanalysis including only patients who underwent primary LRYGB found similar differences between patients with and without a complication. Patients with a short-term complication had significant higher %EWL, six months and one year after bariatric surgery. However, no effect of complications was seen on BMI loss or TWL at both follow-up moments. In addition, after correction for multiple testing, no effect of Clavien-Dindo severity was seen on BMI loss, %EWL or TWL at six months and one year follow-up. Results are displayed in **Table 3**.

Analysis between primary and revisional LRYGB

Comparing primary and revisional LRYGB regardless the occurrence of complications, patients undergoing primary surgery had a significant higher BMI loss, %EWL and TWL than patients undergoing revisional surgery ($p<0.001$; **Table 4**). After one year, the mean %EWL of patients undergoing revisional surgery was 58.1 (SD 25.0), whereas this was 68.4 (SD 20.2) in the primary surgery group. When patients with complications were excluded, the difference between weight loss in terms of BMI loss, %EWL and TWL remained statistical significant with all p-values < 0.001 respectively.

Table 4 - Analysis weight loss primary and revisional bariatric surgery

Postoperative outcome	Primary surgery (n =788; n =771)	Revisional surgery (n =179; n =175)	p–value†
BMI (kg/m^2) loss 6 months (SD)	10.6 (3.1)	7.7 (3)	<0.01
BMI (kg/m^2) loss 1 year (SD)	13.4 (4)	9.2 (3.9)	<0.01
%EWL 6 months (SD)	54.6 (16.8)	48.1 (19.9)	<0.01
%EWL 1 year (SD)	68.4 (20.2)	58.1 (25)	<0.01
TWL (kg) 6 months (SD)	30.5 (9.6)	21.5 (8.5)	<0.01
TWL (kg) 1 year (SD)	38.4 (12.5)	25.9 (11)	<0.01

BMI = Body Mass Index; EWL = Excess Weight Loss; SD = Standard Deviation; TWL = Total Weight Loss

† *Independent sample T test*

Multivariable linear regression analysis

The predictive value of short-term complications on one year %EWL was evaluated through a multivariable linear regression analysis. Adjusted for factors that are associated with postsurgical weight loss, short-term complications are a no significant predictor for one year %EWL (p = 0.075; **Table 5**).

Table 5 - Multivariable linear regression model

Variable	B	SE	p–value
Constant	77.670	2.540	0.000
Short term complication (no=0; yes=1)	4.326	2.423	0.075
Gender (male=0; female=1)	-0.365	2.170	0.866
Age (≤44 years =0; >45 years=1)	-2.934	1.547	0.058
BMI (<50 kg/m^2=0; ≥50 kg/m^2=1)	-14.914	1.985	0.000
Waist circumference (<130cm=0; >131cm=1)	-5.094	1.717	0.003
Revisional surgery (no=0; yes=1)	-16.377	2.385	0.000
AHI (<15/hour=0; ≥15/hour=1)	-0.013	1.745	0.994
Overall type II diabetes (no=0; yes=1)	-5.599	1.662	0.001

AHI = Apnea-Hypopnea-Index; B = Regression coefficient; BMI = Body Mass Index; SE = Standard Error

DISCUSSION

This study evaluated the prevalence of early postoperative complications and its effect on subsequent weight loss, six months and one year after bariatric surgery. Postoperative weight loss was not clearly influenced by early postoperative complications. A difference regarding %EWL was seen after surgery with patients suffering from complications having a higher %EWL. Although a trend was seen toward higher BMI loss and TWL in the complication group after six months ($p = 0.080$ and $p = 0.074$ respectively), this effect was not seen at one year follow-up. While performing similar analysis in primary LRYGB patients, %EWL was likewise higher in the complication group, whereas no difference was detected regarding BMI loss and TWL. In addition, Clavien-Dindo severity had no effect on any definition of weight loss in both overall and only primary LRYGB group, at both follow-up moments. As the preoperative BMI and postoperative BMI loss and TWL were not different between patients with and without a complication, the significant difference of %EWL between groups is of small clinical value. Moreover, when corrected for other factors, that are associated with weight loss[15], short-term complications were no strong predictor for %EWL, one year after surgery. However, as the regression coefficient was 4.326 and the p-value 0.075, a trend was seen towards more weight loss within the complication group. Although weight loss might be higher in the complication group, current study results can conclude that complications do not negatively alter the postoperative outcome in terms of weight loss. Longer hospitalization and enteral or parental nutrition might influence weight loss. Moreover, patients with a complication might require higher energy level to cure from there complication, leading to more weight loss.

In the first 30-day postoperative period, the overall complication rate was 115 (10.2%) which is comparable to literature (early over all complication rate is between the 4.3 and 14.5%)[4;5]. The severe complication rate was also equal to the literature with severe complications occurring in 48 patients (4.2%)[6;7].

Bariatric surgery is regarded successful when at least 50% EWL is reached[16]. Weight loss is associated with several factors, such as a higher preoperative BMI, elder age, type II diabetes, a lower waist circumference, psychological factors, and pouch size[16-18]. Some studies found that the development of postoperative complications is associated with a higher BMI, male gender, hypertension and type of surgery[19;20]. This was not found in the analysis of the baseline characteristics of the present study.

Separate analysis of patients undergoing primary versus revisional surgery showed a, not surprisingly, significant difference in terms of weight loss six months and one year postoperatively. However, the mean %EWL of patients undergoing revisional surgery after one year was still 58%, meaning sufficient weight loss. Although known for a higher complication rate, revisional surgery is proven effective in other studies and the present study as well[8;9;21].

This study has several limitations. At first, although a large, single institution cohort, the severe complication rate of 4.2% comprised only 48 patients. Although not significant, slightly higher weight loss, including BMI loss, %EWL and TWL, was seen in patients with severe complications (Clavien-Dindo ≥ 3). As this is a small sample size with only 48 severe complications, same analysis in a larger cohort could show significant differences regarding weight loss between those patients with- and without a short-term complication. In addition, this study did not evaluate several complication-accompanying factors that might influence postsurgical weight loss. It would be interesting to inventory the effect of duration of hospitalization, readmissions, visits to the emergency department, and the need for enteral of parenteral nutrition on weight loss after bariatric surgery. Including these factors in prospective, larger studies could provide interesting information to the current knowledge. Finally, a subanalysis was performed to assess the occurrence of long term complications. This analysis showed that a history of a short-term complication increased the risk of a complication in the long-term ($p = 0.035$, Odd's ratio 1.827 (95% confidence interval 1.044-3.197), which occurred in 105 (9.3%) patients. However, one year follow-up is not sufficient regarding the long-term complication risk. Although in the present study weight loss was assessed after a maximum of one year follow up, the long-term complications occurred in a longer timeframe post-surgery, with the longest follow-up within this cohort being seven years. Therefore, statements regarding the influence of short-term complications on the development of long-term complications should be addressed in a different study.

In conclusion, the present study shows that weight loss is not negatively influenced by postoperative complications.

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Predictive factors for insufficient weight loss after bariatric surgery: does obstructive sleep apnea influence weight loss?

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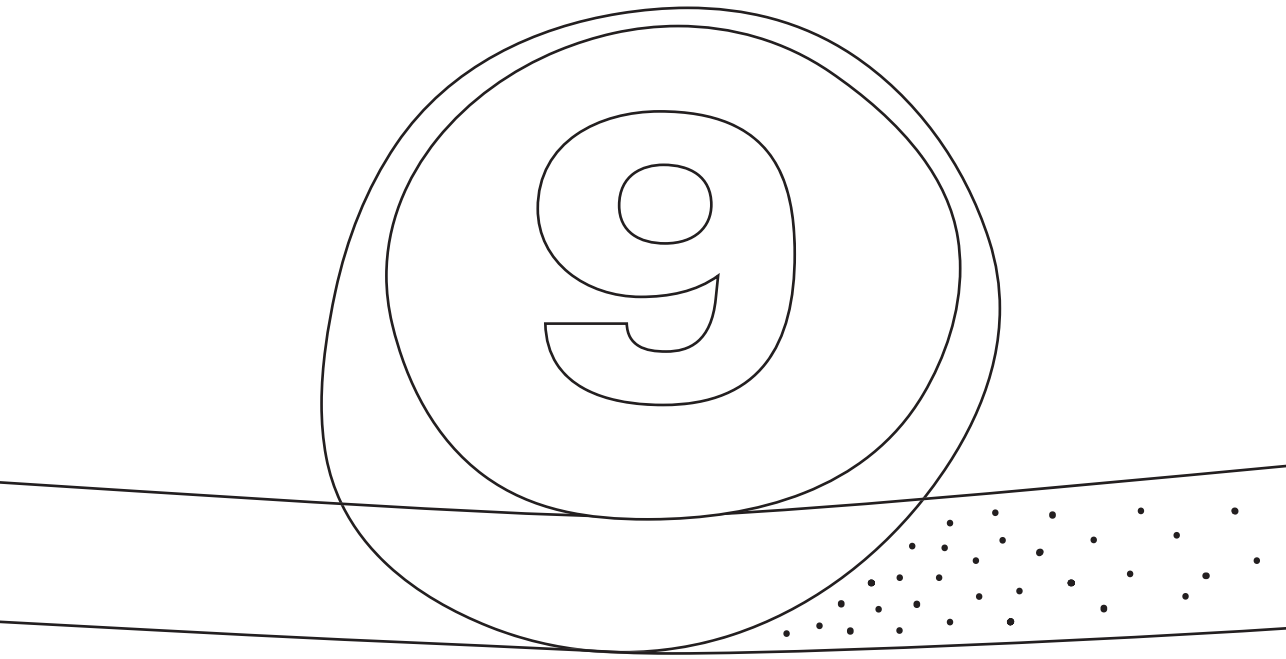

ABSTRACT

Introduction: Important endpoints of bariatric surgery are weight loss and improvement of comorbidities, of which obstructive sleep apnea (OSA) is one of the highest accompanying comorbidities (70%). This study aimed to evaluate the influence of OSA on weight loss after bariatric surgery and to provide predictive factors for insufficient weight loss (defined as ≤ 50% excess weight loss (EWL)) at one-year follow-up.

Methods: All consecutive patients, who underwent primary laparoscopic Roux-en-Y gastric bypass or laparoscopic sleeve gastrectomy between 2006 and 2014, were retrospectively reviewed. Patients with data on preoperative apnea-hypopnea-index (AHI) and pre- and postoperative body mass index (BMI) were included. After surgery, the percentage EWL and BMI changes were compared between preoperatively diagnosed OSA-, subdivided in mild, moderate and severe OSA, and non-OSA patients. Multivariable logistic regression analysis evaluated predictive factors for ≤ 50% EWL.

Results: A total of 816 patients, 522 (64%) with- and 294 (36%) without OSA, were included. After one year, OSA patients achieved less %EWL than non-OSA patients (65.5 SD 20.7 versus 70.3 SD 21.0; $p < 0.01$). The lowest %EWL was seen in severe OSA patients (61.7 SD 20.2). However, when adjusted for waist circumference, BMI and age, no effect of OSA was seen on %EWL or changes in BMI. Although AHI, gender, age, BMI, type of surgery and type II diabetes were predictive factors for ≤ 50% EWL (area under the curve 0.778), the AHI as variable was of little importance.

Conclusion: The presence of OSA does not individually impair weight loss after bariatric surgery.

INTRODUCTION

Obesity affects more than one-third of the North-American population[1] and has proven to be a threat to human health as it predisposes for metabolic syndrome, cardiovascular diseases and other comorbidities[2]. Since bariatric surgery is the only proven effective therapy for morbid obesity, concerning weight loss and improvement of comorbidities in the long term, it is not surprising that the number of bariatric procedures has increased enormously in the last decade.

The two most performed bariatric procedures are the laparoscopic Roux-en-Y gastric bypass (LRYGB; 47%) and laparoscopic sleeve gastrectomy (LSG; 28%)[3]. These procedures result in 66 and 59 percent excess weight loss (%EWL), respectively[4-5].

Despite these good long term results, it is estimated that 10-20% of patients show insufficient weight loss[6-8]. Although little is known about predictive factors for insufficient weight loss, the problem is thought to be multifactorial, including medical, surgical and psychological aspects[8]. Several articles reported a possible association between suboptimal weight loss and high preoperative body mass index (BMI), personality disorders and type II diabetes[6;9-11]. A previous published multivariable logistic regression analysis showed that young patients with a lower BMI and higher waist circumference achieved more %EWL after one year and the success percentage of more than 60% EWL was higher[12]. Another study revealed that early postoperative weight loss predisposes the final result as patients who achieved less than 30% EWL after six months were not likely to achieve more than 50% EWL after two years[13].

Although some predictive factors were found for insufficient weight loss after bariatric surgery, many factors that are common in bariatric surgery patients have not been fully investigated yet. One of them includes obstructive sleep apnea (OSA), one of the highest accompanying comorbidities[14;15]. Ravesloot et al. performed a prospective observational study in which all patients scheduled for bariatric surgery underwent mandatory polysomnography (PSG). With an absolute incidence of 70%, it was concluded that OSA is under recognized and underdiagnosed in patients undergoing bariatric surgery[14]. The advantages of bariatric surgery regarding OSA are described by the systematic review and meta-analysis of Buchwald et al., showing decrease in severity of OSA in 80% of the patients after surgery[16].

However, other studies suggest that OSA itself may cause weight gain in the non-bariatric population due to an associated relationship with obesity, comorbidities and other physiological and metabolic diseases[17]. This could be a result of reduced physical activity and subtle hormonal (leptine and ghrelin) disturbances, leading to an increased appetite[18].

So, while obesity might lead to OSA, OSA might also induce weight gain. To what extent OSA is a risk factor for insufficient weight loss after bariatric surgery is unknown. Therefore, the primary aim of this study is to investigate the %EWL and changes in BMI between OSA and non-OSA patients six months to one year after bariatric surgery. Secondary aims are examining the influence of both OSA severity and CPAP compliance on weight loss and to provide predictive factors for insufficient weight loss (defined as ≤ 50% EWL) after one year follow-up.

METHODS

Study design and study population

A retrospective study was performed with a hospital database in which all patients scheduled for bariatric surgery were entered consecutively. All patients met the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) criteria[19] for bariatric surgery. Patients who underwent primary LRYGB or LSG where considered eligible for inclusion. They were included in this study when the following data were available: 1. length, preoperative weight, preoperative apnea-hypopnea-index (AHI) data; 2. postoperative weights at six months to one-year follow-up. Exclusion criteria were other bariatric procedures, such as laparoscopic adjustable gastric banding (LAGB), revisional surgery from previous bariatric procedures or unavailable data regarding P(S)G and/or pre- and postoperative weights.

Surgical procedures

All LRYGB and LSG procedures were performed by four experienced bariatric surgeons or under their direct supervision, using a standardized technique. Five trocars were used for surgery. The LRYGB consists of two anastomosis, of which the proximal gastrojejunostomy (GJ) was created by the gastric pouch, consisting of an estimated 30 ml volume, and the proximal jenunal limb, whereas the distal jejunojejunostomy (JJ) was created at an estimated 120-150cm distance from the GJ. Both anastomoses were made using staplers and VICRYL 2.0 (Ethicon inc. a Johnson and Johnson Company, Somerville, NY, USA) or a V-loc™ (Covidien, Dublin, Ireland). The LSG was performed with staplers using a 34F nasogastric tube as boogie size. The remnant stomach was removed. Desufflation and skin closure followed after both procedures.

Evaluation obstructive sleep apnea

Preoperative P(S)G provided the AHI, classifying the OSA severity. An AHI of 0-5/hour states no OSA, whereas 5-15/hour, 15-30/hour and ≥ 30/hour states mild, moderate and severe OSA, respectively. Before 2012, preoperative P(S)G was not performed routinely, whereas from 2012 onwards, all patients who were scheduled for bariatric surgery underwent mandatory P(S)G, preoperatively. Since a PSG not only provides the AHI, but also includes a hypnogram showing the sleep cycles, REM sleep, deep sleep, arousal index and awakenings, PSG was preferably performed. However, due to cost reasons, many patients underwent PG that provided the AHI without showing a hypnogram. In case of moderate to severe OSA (AHI ≥ 15/hour), CPAP therapy was prescribed. AHI on CPAP was registered, as well as mean duration of CPAP use per night. Patients were considered CPAP dependent when using the therapy for more than four hours a night, at least 70% of the nights[20]. After surgery, patients with severe OSA were continuously monitored at the Intensive Care Unit during the first night, whereas all other patients (AHI 0-30/hour) were admitted to the bariatric

surgical ward for standard intermittent monitoring. If CPAP therapy was prescribed in patients with an AHI between 15 and 30/hour, they were required to bring their CPAP mask to the bariatric surgical ward for mandatory usage.

Weight loss

The primary endpoint of this study is the %EWL after six months and one year of follow-up. This was calculated based on the pre- and postoperative BMI at six months and one year after bariatric surgery. Changes in BMI were calculated and displayed as differences in BMI points.

Data collection and statistical analysis

Required data were retrieved from patient medical records. The retrieved baseline characteristics included gender; age; preoperative BMI; waist circumference; type of surgery; type II diabetes; hypertension; dyslipidemia; alcohol and smoking. Continuous characteristics of OSA and non-OSA patients were documented with mean/standard deviation and compared with the independent t-test. Normality was evaluated with histograms and the Kolmogorov-Smirnov test. Categorical variables were compared with chi-square test. In addition, baseline characteristics were compared between all OSA severity groups with One-way ANOVA. Homogeneity of variance between groups (ANOVA assumption) was tested by using Levene's test. Comparison of %EWL and BMI changes were primarily completed between non-OSA (AHI < 5/hour) and OSA (AHI ≥ 5/hour) groups with the independent t-test. Analysis for %EWL and BMI changes between all OSA severity groups was achieved with One-way ANOVA with post-hoc analysis and Bonferroni correction. Potential influence of confounders was investigated with covariance analysis. Within the CPAP group, comparison of %EWL and BMI changes between compliant and non-compliant patients was achieved with independent t-test.

Finally, correlations between AHI and %EWL and loss of BMI points were analyzed with Pearson's correlation coefficients. A prediction model for insufficient %EWL, defined as EWL ≤50%, was created by multivariable logistic regression analysis according to the TRIPOD statement[21].

All data were anonymously entered in a database. The local ethical committee of the Director board of the hospital provided approval for this study.

RESULTS

Patient characteristics

From November 2007 until January 2014, 1594 patients underwent bariatric surgery. Of these patients, 973 underwent primary LRYGB or primary LSG. After excluding 157 patients (16%) due to missing data, concerning P(S)G and/or weight data, a total of 816 patients were included for analysis. OSA was diagnosed in 522 (64%) patients, of which 163 (31%) had a severe form.

The mean AHI of the entire study population was 18.9 /hour (24). Patients without OSA had a mean AHI of 2.3/hour (1.5), whereas patients with OSA had a mean AHI of 28.2 /hour (25.6). Mild, moderate and severe OSA patients had an AHI of 9/hour (2.8), 21.2/hour (4.2) and 59.4/hour (24.2), respectively. A total of 275 (33.7%) patients received CPAP therapy prior to surgery. Significant differences between OSA and non-OSA patients were found for the variables gender, age, preoperative BMI, waist circumference, type II diabetes, hypertension and dyslipidemia. Baseline characteristics and their comparisons among the different OSA groups are shown in **Table 1**.

Influence of OSA on weight loss

Six months after bariatric surgery, the entire study population showed a mean EWL of 54.1% (16.9) (**Table 2**). A trend was seen towards less %EWL in patients with OSA when compared to patients without OSA (53.2% versus 55.6%; $p = 0.058$).

One-year post-surgery, mean EWL of the whole cohort was 67.2% (20.9). Significant less %EWL was seen in OSA patients when compared to non-OSA patients (65.5% versus 70.3%; $p < 0.01$).

At both intervals, %EWL was significantly different between patients without OSA, mild OSA, moderate OSA and severe OSA ($p < 0.01$). After six months, post-hoc analysis with correction for multiple testing showed that this was a result of a significant difference of %EWL between patients without OSA and those with severe OSA ($p < 0.01$). Comparing mild and moderate OSA patients with severe OSA patients revealed post-hoc p-values of 0.058 and 0.056 respectively. At one-year follow-up, post hoc-analysis as previously described showed significantly less %EWL in severe OSA patients when compared with patients without OSA ($p < 0.01$) and those with mild OSA ($p = 0.015$).

Three confounders, including waist circumference, BMI and age influenced these results. When adjusted for these confounders, a significant difference between OSA severity groups was found six months after surgery ($p = 0.015$), whereas this difference was not presented anymore at one-year follow-up ($p = 0.781$).

In all OSA severity groups the expected increase of %EWL was significant between six months and one year after surgery ($p < 0.01$).

In addition to the %EWL, changes in BMI were calculated. After six months, mean BMI loss was 10.7 (3.1). After one year, mean BMI loss was 13.3 (4.1). No clinical significant difference was found between OSA and non-OSA patients, or between all OSA severity groups at both intervals (**Table 2**).

Table 1 - Comparison of baseline characteristics; OSA and non-OSA patients

Variables	All patients n = 816	No OSA AHI < 5 n = 294	OSA AHI ≥ 5 n = 522	p value	Mild OSA AHI 5-15 n = 209	Moderate OSA AHI 15-30 n = 150	Severe OSA AHI ≥ 30 n = 163	p value*
Gender; n (%)				< 0.01[1]				< 0.01[1]
Female	654 (80.1)	272 (92.5)	382 (73.2)		187 (89.5)	115 (76.7)	80 (49.1)	
Male	162 (19.9)	22 (7.5)	140 (26.8)		22 (10.5)	35 (23.3)	83 (50.9)	
Age; years (SD)	44.4 (10.6)	39.7 (9.8)	47.1 (10.2)	< 0.01[2]	44.3 (10.6)	47.8 (9.6)	49.9 (9.2)	< 0.01[3]
Preoperative BMI; kg/m² (SD)	45.8 (6.7)	44.4 (5.7)	46.5 (7.2)	< 0.01[2]	45.3 (6.4)	46.2 (7.2)	48.4 (7.7)	< 0.01[3]
Waist circumference; cm (SD)	131.5 (15.2) (n = 718)	126.9 (13.4) (n = 264)	134.2 (15.5) (n = 454)	< 0.01[2]	129 (14.1) (n = 194)	135.1 (15) (n = 127)	140.9 (15.6) (n = 133)	< 0.01[3]
Type of surgery; n (%)				0.127[1]				0.221[1]
LRYGB	766 (93.9)	281 (95.6)	485 (92.9)		198 (94.7)	137 (91.3)	150 (92)	
LSG	50 (6.1)	13 (4.4)	37 (7.1)		11 (5.3)	13 (8.7)	13 (8)	
Type II diabetes; n (%)	250 (30.6)	61 (20.7)	189 (36.2)	< 0.01[1]	54 (25.8)	60 (40)	75 (46)	< 0.01[1]
Hypertension; n (%)	359 (44)	90 (30.6)	269 (51.5)	< 0.01[1]	86 (41.1)	82 (54.7)	101 (62)	< 0.01[1]
Dyslipidemia; n (%)	227 (27.9)	61 (20.8)	166 (31.8)	< 0.01[1]	51 (24.4)	48 (32)	67 (41.1)	< 0.01[1]
Alcohol; n (%)	332 (42)	128 (44.3)	204 (40.6)	0.316[1]	77 (37.4)	66 (45.8)	61 (40.1)	0.319[1]
Smoking; n (%)				0.311[1]				0.698[1]
Yes	156 (19.5)	62 (21.5)	94 (18.4)		36 (17.6)	26 (17.8)	32 (20.1)	
Former	173 (21.7)	55 (19)	118 (23.1)		49 (23.9)	30 (20.5)	39 (24.5)	

AHI = Apnea Hypopnea Index; BMI = Body Mass Index; LRYGB = Laparoscopic Roux-en-Y Gastric Bypass; LSG = Laparoscopic Sleeve Gastrectomy; OSA = Obstructive Sleep Apnea

[1] Chi-square test; [2] Independent t-test; [3] One-Way ANOVA

* p value between all OSA severity groups, including no-, mild-, moderate- and severe OSA

The AHI and %EWL showed a Pearson correlation of -0.149 ($p < 0.01$) and -0.184 ($p < 0.01$) after six months and one year respectively. The %EWL decreases as AHI increases. At six months, a higher AHI resulted in less BMI changes (Pearson correlation 0.105; $p < 0.01$). No significance level was reached after one year (Pearson correlation 0.06; $p = 0.097$).

Influence of CPAP compliance on weight loss

Preoperatively, CPAP was prescribed in 275 OSA patients (52.7%), of which four (1.9%), 112 (74.7%) and 159 (97.5%) patients were diagnosed with mild, moderate and severe OSA, respectively. The four patients with mild OSA received CPAP treatment due to clinical symptoms or severe positional OSA, meaning the AHI increases when a patient sleeps in supine position. This number (n=4) was too small to analyze the effect of CPAP compliance on %EWL and these four patients were therefore excluded from analyses. Postoperative CPAP compliance was objectified in 140 moderate and severe patients. Compliance reports were not available of 131 patients. Reasons were returned CPAP devices without previous compliance reports, no response of the patients after repeated invitations for follow-up or prescribed CPAP elsewhere.

The mean AHI on CPAP was 3.8 (3.9). Median duration per night of CPAP usage was 224 (520) minutes. No difference in %EWL or BMI loss between compliant and non-compliant CPAP use was found in both moderate and severe OSA patients (Table 3). Although a positive correlation was found between average minutes CPAP use and %EWL at six months (Pearson correlation 0.196, $p = 0.040$), no correlation was detected after one year of follow-up ($p = 0.113$). In addition, no significant correlation was found between average CPAP use and BMI changes at both follow-up moments ($p = 0.318$ and $p = 0.641$ respectively).

Weight loss and postoperative AHI six months and one year after bariatric surgery

Preoperatively, a total of 522 patients had OSA, of which the median AHI was 18.9/hour (144). Six months after bariatric surgery, 112 moderate and severe OSA (35.8%) patients repeated their P(S)G, showing a significant decrease of the median AHI to 10.4/hour (IQ range 14.4; $p < 0.01$). OSA (AHI ≥5/hour) was still present in 86 (76.8%) patients, showing a median AHI of 13.4/hour (IQ range 15.5). Consequently, 26 patients had remission of OSA (AHI 2.9/hour IQ range 1.8). Patients with persistent OSA had similar %EWL as those with remission of OSA (51.8 SD 15.8 versus 57.1 SD 15.1, $p = 0.131$). In addition, mean BMI loss was also comparable between groups (11.2 SD 3.1 versus 11.2 SD 2.9; $p = 0.995$).

Of the 112 moderate and severe OSA patients who repeated P(S)G, 76 patients (67.9%) were downgraded to no or mild OSA and no longer required CPAP therapy. Consequently, 36 patients (32.1%) still had an AHI above fifteen, requiring CPAP therapy.

Table 2 – Weight Loss in OSA and non-OSA patients displayed in %EWL and changes in BMI

Variables	All patients	No OSA AHI 0-5	OSA AHI ≥ 5	p value	Mild OSA AHI 5-15	Moderate OSA AHI 15-30	Severe OSA AHI ≥ 30	p value**
%EWL 6 months (SD)	54.1 (16.9)	55.6 (16.2)	53.2 (17.2)	0.058[1]	54.6 (17.3)	55.0 (17.8)	49.9 (16.3)	< 0.01[2]
Adjusted *	-	52.1	-	-	53.7	57.2	55.7	0.015
%EWL 1 year (SD)	67.2 (20.9)	70.3 (21.0)	65.5 (20.7)	< 0.01[1]	68.5 (20.9)	65.4 (20.5)	61.7 (20.2)	< 0.01[2]
Adjusted *	-	66.6	-	-	67.9	68.7	68.0	0.781
Δ BMI 6 months (SD)	10.7 (3.1)	10.4 (3.0)	10.8 (3.1)	0.049[1]	10.6 (3.0)	11.0 (3.0)	11.0 (3.4)	0.120[2]
Δ BMI 1 year (SD)	13.3 (4.1)	13.1 (4.0)	13.4 (4.1)	0.466[1]	13.3 (3.9)	13.1 (3.9)	13.6 (4.6)	0.592[2]

AHI = Apnea Hypopnea Index; EWL = Excess Weight Loss; FU = Follow Up; OSA = Obstructive Sleep Apnea; SD = Standard Deviation
[1] Independent t-test; [2] One-way ANOVA; * %EWL adjusted for waist circumference, BMI and age (n=689)
** p value between all OSA severity groups, including no-, mild-, moderate- and severe OSA; Homogeneity of variances; Levene's test p > 0.05
Δ Changes in BMI points

Table 3 – Weight Loss in CPAP compliant and non-compliant patients

Variables	Moderate OSA; CPAP compliant *(n=20)*	Moderate OSA; CPAP non-compliant *(n =41)*	p value	Severe OSA; CPAP compliant *(n =26)*	Severe OSA; CPAP non-compliant *(n =53)*	p value
%EWL 6 months	55.9 (18.9[a])	55.3 (18.8[a])	0.944[1]	50.8 (15.4[a])	48.8 (17.5[a])	0.620[1]
%EWL 1 year	67.4 (21.4[a])	66.8 (21.4[a])	0.454[1]	61.4 (17.1[a])	61.7 (20.2[a])	0.950[1]
Δ BMI 6 months	10.6 (3.3[a])	10.7 (2.7[a])	0.918[1]	11.5 (3.0[a])	10.9 (3.8[a])	0.438[1]
Δ BMI 1 year	12.5 (3.8[a])	13.3 (4.0[a])	0.915[1]	13.9 (3.5[a])	13.8 (4.9[a])	0.930[1]

AHI = Apnea Hypopnea Index; CPAP = Continuous Positive Airway Pressure; EWL = Excess Weight Loss; OSA = Obstructive Sleep Apnea
[1] Independent t-test; [a] Standard deviation; Δ Changes in BMI points

One year after surgery, 55 patients repeated their P(S)G, showing a median AHI of 7.5/hour (IQ range 9.8). These P(S)Gs revealed that OSA still existed in 38 (69%) patients, whereas remission was reported in 17 (31%) patients. The AHI of these groups were 10.1/hour (91) and 2.7/hour (4.7), respectively. No significant difference of %EWL was seen between patients with remission of OSA and those with persistent OSA (64.7 SD 15.9 versus 57 SD 17.8; p = 0.123). In addition, no difference regarding BMI changes was detected between persistent OSA (13 SD 5.5) and cured OSA (13.7 SD 3.4) patients (p = 0.574).

Of the 55 moderate and severe OSA patients repeating P(S)G after one year, the AHI downgraded below fifteen in 42 patients (76.4%), who consequently no longer required CPAP therapy. An AHI above fifteen was still presented in 13 patients (26.3%), who were advised to continue CPAP therapy.

Predictors for insufficient weight loss after bariatric surgery (≤ 50% EWL)

A total of 149 (19.7%) patients had less than 50% EWL one year after bariatric surgery. In univariate logistic regression analysis, variables gender, age, BMI, waist circumference, AHI, type II diabetes, hypertension and dyslipidemia reached a p-value <0.1 (**Table 4**).

Table 4 - Univariate logistic regression analysis; predictors for ≤ 50% EWL

	≤ 50% EWL - 1 year after bariatric surgery		
Variable	OR	95% C.I.	p value
Gender			
Female			
Male	1.711	1.127-2.600	0.012
Age; years	1.024	1.006-1.041	0.008
Preoperative BMI; kg/m²	1.127	1.095-1.159	0.000
Waist circumference; cm	1.047	1.033-1.061	0.000
AHI	1.011	1.004-1.017	0.002
Type of surgery	3.864		
LRYGB			
LSG		2.122-7.037	0.000
Type II diabetes	1.723	1.186-2.504	0.004
Hypertension	1.395	0.974-1.999	0.069
Dyslipidemia	1.623	1.107-2.379	0.013
Alcohol	1.129	0.780-1.635	0.519
Smoking			
Yes	0.812	0.490-1.346	0.419
Former	1.091	0.695-1.711	0.705

AHI = Apnea Hypopnea index; BMI = Body Mass Index; C.I. = Confidence Interval; EWL = Excess Weight Loss; LRYGB = Laparoscopic Roux-en-Y Gastric Bypass; LSG = Laparoscopic Sleeve Gastrectomy; OR = Odds Ratio; OSA = Obstructive Sleep Apnea

Multivariable logistic regression analysis evaluated predictive factors for ≤ 50% EWL, one year after bariatric surgery. All characteristics, including gender, age, preoperative BMI, waist circumferences, AHI, type of surgery, type II diabetes, hypertension, dyslipidemia, alcohol and smoking were analyzed. All continuous variables were linear related to the outcome.

Multivariable analysis with backward selection resulted in the elimination of the variables waist circumference, smoking, hypertension, dyslipidemia and alcohol, consecutively. The optimal prediction model included gender, age, preoperative BMI, preoperative AHI, type of surgery and type II diabetes (Nagelkerke R square 0.208, Hosmer and Lemeshow test p=0.443, AUC 0.77, Figure 1) (Table 5).

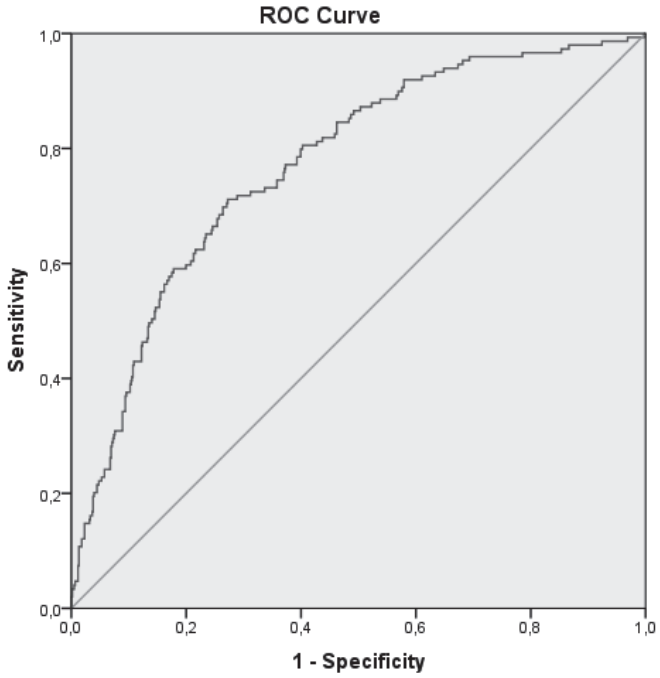

Figure 1 – ROC curve for prediction model for insufficient (≤ 50% EWL) weight loss
Area under the curve: 0.771
Standard Error: 0.021
p < 0.01
95% C.I. 0.729-0.812

Table 5 - Multivariable logistic regression analysis; predictors for ≤ 50% EWL

	≤ 50% EWL - 1 year after bariatric surgery		
Variable	OR	95% C.I.	p value*
Gender; F/M			
Male	1.645	0.934-2.868	0.080
Age; years	1.035	1.011-1.058	0.003
BMI; kg/m²	1.148	1.108-1.190	0.000
AHI	0.992	0.982-1.002	0.117
Type of surgery; LRYGB/LSG			
LSG	1.961	0.918-4.187	0.082
Type II diabetes	1.921	1.199-3.076	0.007

AHI = Apnea Hypopnea index; BMI = Body Mass Index; C.I. = Confidence Interval; EWL = Excess Weight Loss; LRYGB = Laparoscopic Roux-en-Y Gastric Bypass; LSG = Laparoscopic Sleeve Gastrectomy

*Hosmer and Lemeshow test: $p > 0.05$

Nagelkerke R square: 0.208

DISCUSSION

Study population

In this bariatric surgery population, OSA was diagnosed by P(S)G in 522 (64%) patients, of which 163 (31%) suffered of a severe form. This high rate is in agreement with literature, showing a prevalence of 70% and 40%, respectively[14].

The role of OSA in weight loss after bariatric surgery

After bariatric surgery, a significant difference in %EWL between OSA severity groups was seen at both six months and one-year follow-up. These differences were caused by a lower %EWL in severe OSA patients. However, these results were not significant after adjusting for waist circumference, BMI and age. In combination with many significant differences in baseline characteristics of OSA severity groups, less %EWL is likely to be caused by higher BMI (correlation -0.478; $p < 0.01$), higher waist circumference (correlation -0.381; $p < 0.01$); older age (correlation -0.098; $p < 0.01$); presence of type II diabetes (mean EWL 63.1% SD 20.9 versus 69.0% SD 20.7; $p < 0.01$); hypertension (mean EWL 65.3% SD 21.7 versus 68.7% SD 20.2; $p = 0.028$) and dyslipidemia (mean EWL 63.6% SD 21.3 versus 68.6% (20.6); $p < 0.01$). Therefore, it can be concluded that the less %EWL in OSA patients compared to non-OSA patients is more accountable to its accompanying characteristics than to the AHI itself. Furthermore, no difference regarding BMI changes was detected between patients with and without OSA. Results of this study imply that the importance of OSA regarding weight loss is weak and perhaps transient.

However, moderate and severe OSA patients were treated with CPAP, which reduces the AHI below five. It could be hypothesized that when CPAP is compliantly used, OSA itself no longer influences the %EWL or changes in BMI. The effect of CPAP compliance is therefore an interesting topic for future prospective studies. Although no difference was detected between CPAP compliant and non-compliant OSA patients in this study, a weak positive correlation was found between average CPAP use and %EWL six months after surgery. This implies that more compliant CPAP use provides more %EWL. However, CPAP compliance was not always objectified during the relevant follow-up period, but at a random period after surgery. This may influence results, as CPAP compliance may vary during follow-up. In addition, no correlation was detected between average CPAP use and %EWL or changes in BMI, one-year post-surgery. In order to conclude whether CPAP compliance has a significant effect on weight loss, prospective studies are required evaluating the mean compliance during the relevant follow-up period.

While a significant correlation of AHI and %EWL was found, Pearsons' rho was only -0.185, implying a weak correlation. In univariate analysis, the AHI explained 2% of ≤ 50% EWL after one-year follow-up. One of the limitations of the present study is the discrepancy between the performance of PSG and PG due to cost reasons. There can be substantial differences in AHI between PSG and PG. As PSG includes sleep/wake

periods, the total AHI is based on the AHI in sleeping periods, whereas PG measures the average AHI during the whole night without differentiating between sleep/wake periods. Since the AHI is zero during wake periods, patients who underwent PG instead of PSG may have a reported AHI that underestimated the true AHI. For this reason, a subanalysis was performed. Of 816 included patients, 476 (58.3%) and 324 (39.7%) underwent PG and PSG respectively. Differentiation between PG and PSG was not possible in 16 patients in whom sleep study was performed elsewhere. Median AHI of PG and PSG was 6.3/hour (IQ-range 15.1) and 14.5/hour (IQ-range 29.5) respectively ($p < 0.01$). Although the performance of PG and PSG might have introduced selection bias to this study, this probably has no effect on current study conclusions. The effect of OSA on %EWL is probably even less than accounted for in the current study, as patients who underwent PG have an underestimated AHI. Moreover, this would be the only selection bias as all patients, including those with and without symptomatic OSA, underwent sleep registration prior to surgery from 2012 onwards. This was never described in literature before.

Although this is the first study investigating the influence of OSA on weight loss in bariatric surgery patients, the exact role of OSA in obesity, weight regain/insufficient weight loss, and the appearance of other related comorbidities such as type II diabetes and hypertension has not fully been investigated, yet. Future research is needed in other to understand the exact physiology of OSA and associated comorbidities. The association between OSA and weight gain might change due to physical and anatomic changes after bariatric surgery. Additionally, as weight loss was only analyzed in the short terms (six months and one year), results on the long term are interesting in future studies.

Predictors for insufficient EWL (≤ 50%)

In multivariable logistic regression analysis, gender, age, preoperative BMI and AHI, type of surgery and type II diabetes appeared to provide the best model prediction insufficient weight loss (≤ 50% EWL). This model explains 21% of ≤50% EWL, one year after bariatric surgery.

Five of these variables, including gender, age, preoperative BMI, type of surgery and type II diabetes, are in agreement with literature[7-8;11-12]. Although waist circumference was found to be a predictor in other studies, this variable gave no improvement to the multivariable model in present study. Perhaps this variable could be added in a prediction model in other study populations or in combination with other variables.

This was the first study that included the AHI in the multivariable regression analysis. Since in the present population preoperative P(S)G was performed in most patients and not only based on questionnaires and/or clinical parameters, the AHI can be regarded as a reliable predictor in the whole study population. Although adding this variable to the model gave improvement of the ROC-curve, the odds-ratio was 0.992, showing a slightly protecting effect for ≤ 50% EWL. This might be result, however, of predictors that are taken over by other characteristics than the AHI or

the chosen definition for insufficient weight loss. By dichotomizing the outcome (≤ 50 or > 50 %EWL), essential information is lost. It can be concluded that the statistical value of OSA in the multivariable predictive equation is weak and that the AHI was not the most prominent variable.

This study provided a non-validated prediction model explaining 20 % of ≤ 50 % EWL, one year after bariatric surgery. This shows that 80 % of ≤ 50 % EWL is explained by other factors. As Karmali et al. reported, the problem of insufficient weight loss is likely to be multifactorial, including medical, surgical and physiological aspects[3]. Future research is required to reveal more predictive factors for insufficient weight loss. In order to provide better preoperative education and awareness, an optimal prediction model needs to be developed.

CONCLUSION

A significant decreased %EWL is seen in OSA patients, especially in those with severe OSA, when compared to patients without OSA, one year after bariatric surgery. However, this effect seems to disappear after correcting for the variables waist circumference, BMI and age, which are correlated with OSA and have a known relationship with postsurgical weight loss. In addition, no difference was detected in mean BMI loss. Six variables including the AHI provided a good prediction model for insufficient weight loss i.e. ≤ 50% EWL (AUC 0.771). Although the statistical value of the AHI was of little importance, the AHI was included in the model as it might have a more prominent role in other or larger cohorts. Therefore, it should be tested in larger (and long term) patient cohorts before its value as a predictor can be assessed. CPAP compliance during the relevant follow-up period should then be assessed as well. With current study results, it can be concluded that OSA itself has no important influence on weight loss after bariatric surgery.

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Impact of obstructive sleep apnea on quality of life after laparoscopic Roux-en-Y gastric bypass

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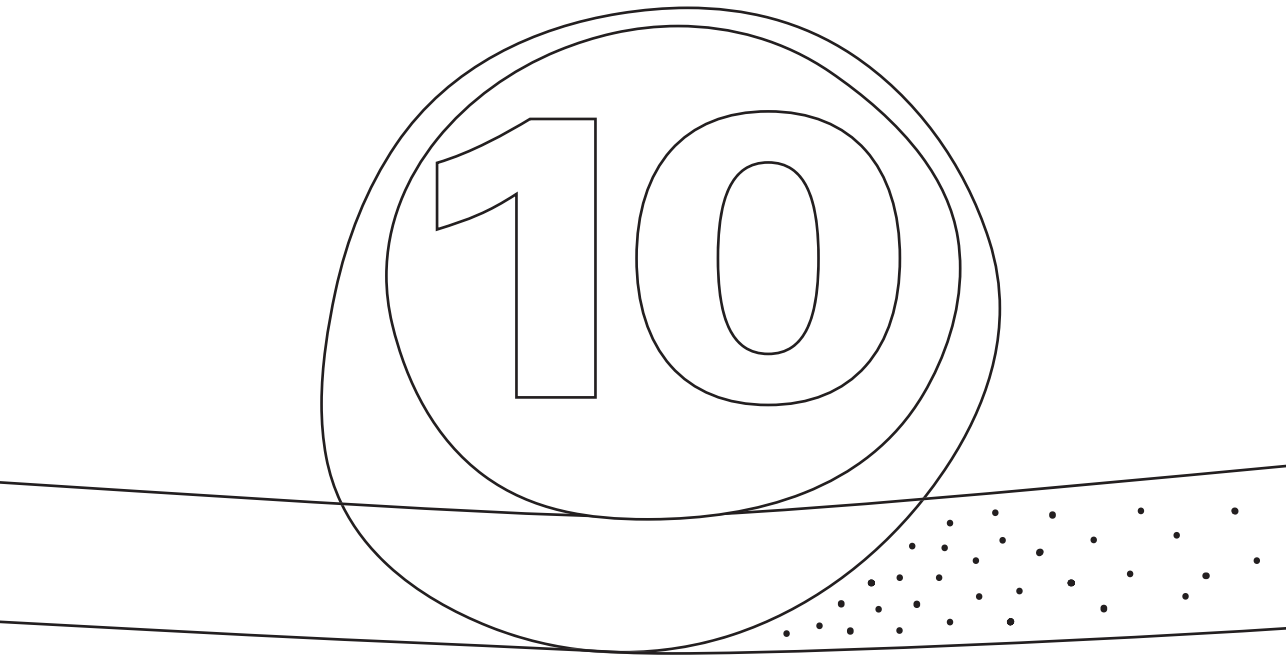

ABSTRACT

Introduction: To examine the influence of obstructive sleep apnea (OSA) on the quality of life (QoL) in bariatric surgery.

Methods: All patients who underwent a laparoscopic Roux-and-Y gastric bypass (LRYGB), preoperative poly(somno)graphy and completed an Impact of Weight on QoL-Lite questionnaire before and after surgery were included.

Results: A total of 276 patients were included. OSA was diagnosed in 150 (53.3%) patients. All subscale scores improved 15 months post-surgery ($p < 0.01$). Total scores improved from 51.2 (SD 19.1) to 89.7 (SD 13.9). Lower postoperative scores were seen in OSA patients on subscales Public Distress (90.4 SD18.8 versus 95.7 SD10.2; p=0.003) and Work (92.9 SD15 versus 96.1 SD9.7; $p = 0.031$). All postoperative subscale scores were negatively correlated with OSA severity ($p < 0.01$).

Conclusion: After LRYGB, QoL improved in both OSA and non-OSA patients. OSA patients, especially patients with severe OSA, have lower postoperative scores on subscales Public Distress and Work after LRYGB.

INTRODUCTION

Obesity is associated with a decreased quality of life (QoL). Bariatric surgery is increasingly being performed to treat the rising epidemic of morbid obesity and has shown to provide a significant improvement of this QoL[1-2]. This improvement has shown to be consequence to both a substantial percentage of weight loss and comorbidity improvement[3-6].

One of the most prevalent comorbidities among morbidly obese subjects is obstructive sleep apnea (OSA)[7]. Although both OSA and QoL independently showed improving trends after bariatric surgery[8-12], few articles have been published evaluating the QoL between bariatric patients with and without OSA. Moreover, these studies show contrasting results and included populations that all lacked mandatory sleep studies to adequately diagnose OSA prior to bariatric surgery[13-17].

Since OSA is independently associated with a diminished QoL due to a consequence of excessive daytime sleepiness and altered circadian rhythms[18], it can be hypothesized that OSA patients have less QoL improvement after bariatric surgery and could therefore benefit from extensive postoperative follow-up and weight loss interventions. Bearing this in mind, the aim of this study is to determine the potential influence of OSA on postoperative QoL.

MATERIAL AND METHODS

We performed a retrospective chart review of consecutive patients who underwent primary laparoscopic Roux-and-Y gastric bypass (LRYGB) in the period February 2012 – January 2014[22]. All patients underwent a LRYGB according to standardized techniques as previously described[23].

Patients were included in the study if they had undergone a preoperative poly(somno)graphy (P(S)G) and completed pre- and postoperative QoL questionnaires. The local ethical committee of the Director board of the Institution provided approval for this study.

QoL questionnaire

Patients were invited to complete an Impact of Weight on QoL-Lite questionnaire at two intervals; six to nine weeks before- and fifteen months after LRYGB.

The questionnaire is a validated 31-item self-report measure of obesity-specific QoL[21]. The total score is subdivided into five domains, representing Physical Function, Self-Esteem, Sexual Life, Public Distress and Work. Scores vary from zero (worst score) to 100 (best score).

Management of OSA

The severity of OSA is expressed in the apnea-hypopnea-index (AHI), representing the number of apneas and hypopneas per hour during sleep. OSA is present if the AHI is ≥ 5/hour. Mild OSA represents an AHI of 5-15/hour; moderate OSA an AHI of 15-30/hour and severe OSA an AHI greater than 30/hour[20].

The diagnosis of OSA is established by sleep studies, including P(S)G. Since 2012, all patients scheduled for bariatric surgery undergo mandatory preoperative P(S)G in our center as previously described[19].

Continuous Positive Airway Pressure (CPAP) was mostly prescribed in those with an AHI ≥ 15/hour. Six to nine months post-surgery, all patients with preoperative CPAP therapy were invited for a second P(S)G, after which was decided whether patients still required CPAP.

Statistical analysis

Pre- and postoperative QoL results were compared with a paired t-test. Scores for every QoL subscale were compared with an independent t-test or one-way ANOVA with correction for multiple testing (Bonferroni). Adding the preoperative QoL score as covariate and performing repeated measures ANOVA equalized baseline QoL. Correlations between preoperative AHI and both pre- and postoperative QoL scores were calculated with Pearson's rho. Finally, a multivariable linear regression model was developed in order to evaluate the effect of OSA on postoperative QoL scores.

RESULTS

Study population

Of the 539 patients who underwent a LRYGB, 482 (89.4%) underwent a preoperative P(S)G. Of these patients, 276 (57.3%) completed a pre- and postoperative QoL questionnaire and were included.

The study population consisted of 240 (87%) women and 36 (13.4%) men. Mean preoperative Body Mass Index was 44.7 (SD 6.1) kg/m² and mean age 43.5 (SD 10.8) years. Preoperatively OSA was diagnosed in 150 patients (54.3%). Median AHI of the entire study population was 6.4/hour (IQR 14.9). Median AHI was 1.7/hour (IQR 2.9) and 15.3/hour (IQR 18.3) in non-OSA and OSA patients, respectively. Patients with mild, moderate and severe OSA had a median AHI of 8.7/hour (IQR 4.8), 18.9/hour (IQR 6.3) and 49.5/hour (IQR 28.6) respectively.

QoL and OSA

All QoL scores significantly improved in both OSA and non-OSA groups post-surgery. **Table 1** displays QoL scores between OSA and non-OSA patients. **Figure 1** illustrates the persistent effect of OSA on two subscales after equalizing preoperative subscale scores.

Evaluating OSA severity groups, Public Distress ($p < 0.01$) and Work ($p < 0.01$) were significantly different postoperatively. After correction for multiple testing, a significant difference between non-OSA and severe OSA groups was seen for the subscales Public Distress (95.7 SD 10.2 versus 86.3 SD 23); $p < 0.01$) and Work (96.1 SD 9.7 versus 89.8 SD 20.9; $p = 0.052$).

Correlation AHI and QoL scores

Preoperatively, no significant correlations were detected between AHI and QoL scores. However, all subscales showed a significant negative correlation after surgery; every score decreases as the AHI increases. The correlation of AHI and Physical Functioning was -0.156 ($p < 0.01$); AHI and Self-Esteem -0.194 ($p < 0.01$); AHI and Sexual Life -0.142 ($p = 0.018$); AHI and Public Distress -0.305 ($p < 0.01$); AHI and Work -0.274 ($p < 0.01$); AHI and Total score -0.238 ($p < 0.01$).

Multivariable linear regression analysis

Table 2 displays the effect of OSA on postoperative Public Distress scores, with correction of potential confounders. The value of OSA was not significant anymore ($p = 0.094$). Similar analyses were achieved for postoperative Work scores. OSA was no longer significant ($p = 0.447$).

Table 1 - Results of IWQoL-Lite scores, pre- and postoperatively

Variables	All patients (n=276) Preop versus Postop		No OSA (n=126) versus OSA (n=150) - Preop			Difference Pre- and Postop No OSA versus OSA			No OSA (n=126) versus OSA (n=150) - Postop		
PF (SD)	39.7 (22.1)	88.9 (15.0)[1]	40.9 (22.1)	38.7 (22.1)	p=0.397[2]	49.4 (22.1)	49.0 (23.2)	p=0.882[2]	90.3 (12.8)	87.7 (16.6)	p=0.141[2]
SE (SD)	49.8 (26.3)	87.7 (18.9)[1]	46.8 (25.4)	52.4 (26.8)	p=0.078[2]	41.5 (26.8)	34.7 (26.8)	p=0.037[2]	88.3 (17.1)	87.1 (20.3)	p=0.603[2]
SL (SD)	54.6 (33.3)	86.8 (22.6)[1]	54.4 (31.7)	54.8 (34.7)	p=0.924[2]	32.8 (32.8)	31.8 (33.3)	p=0.811[2]	87.2 (21.6)	86.6 (23.5)	p=0.835[2]
PD (SD)	60.6 (25.3)	92.8 (15.7)[1]	62.3 (21.9)	59.2 (27.8)	p=0.290[2]	33.3 (21.2)	31.2 (28.0)	p=0.479[2]	95.7 (10.2)	90.4 (18.8)	p=0.003[2]
W (SD)	70.2 (23.1)	94.4 (13.0)[1]	71.8 (22.0)	68.9 (23.9)	p=0.297[2]	24.3 (22.2)	24.0 (22.4)	p=0.898[2]	96.1 (9.7)	92.9 (15.0)	p=0.031[2]
Total (SD)	51.2 (19.1)	89.7 (13.9)[1]	51.4 (18.0)	51.1 (20.0)	p=0.871[2]	39.7 (18.7)	37.5 (20.2)	p=0.356[2]	91.1 (11.2)	88.5 (15.8)	p=0.117[2]

AHI = Apnea Hypopnea Index; OSA = Obstructive Sleep Apnea; PD = Public Distress; PF = Physical Functioning; Postop = Postoperative score; Preop = Preoperative score; SE = Self-Esteem; SL = Sexual Life; Total = Total score; W = Work

[1]Paired t-test: all $p < 0.01$; [2]Independent t-test

Table 2 - Multivariable linear regression analysis for postoperative Public Distress Score

Variables	B	Standard Error	p-value	95% CI
Constant	73.764	4.875	0.000	64.162 - 83.367
Preoperative PD score (≥ 60)*	6.958	1.925	0.000	3.166 - 10.751
OSA	-3.309	1.969	0.094	-7.187 - 0.569
Gender (Female)	6.591	2.978	0.028	0.724 - 12.458
Hypertension	-1.062	2.097	0.613	-5.191 - 3.068
Age (≥ 43 years)*	2.017	2.017	0.318	-1.957 - 5.990
BMI (≥ 40 kg/m^2)**	-0.884	2.635	0.737	-6.074 - 4.305
Waist circumference (≥ 127 cm)*	-0.515	2.092	0.806	-4.636 - 3.605
EWL (≥ 50%)***	14.025	2.669	0.000	8.767 - 19.282

BMI = Body Mass Index; EWL = Excess Weight Loss; OSA = Obstructive Sleep Apnea; PD = Public Distress

* = no normal distributed and therefore divided into two equal groups

** = definition of morbid obesity

*** = international accepted cutoff point for sufficient weight loss

Effect of OSA remission (AHI < 5) on QoL after bariatric surgery

A total of 77 patients were diagnosed with moderate or severe OSA preoperatively and were invited for a postoperative P(S)G. Of these patients, 31 (40.3%) underwent a P(S)G at a mean follow-up of 11.1 (SD 6.3) months. While there was OSA remission (AHI < 5/hour) in 13 (41.9%) patients, 18 (58.1%) patients had persistent OSA (AHI ≥ 5/hour). However, the median AHI of these 18 patients significantly decreased from 33.4/hour (IQR 42) to 8.4/hour (IQR 7.9), p < 0.01. Moreover, only three out of 18 patients still had a CPAP indication at follow-up (AHI ≥ 15/hour).

No significant differences were detected in excess weight loss between patients with OSA remission (AHI < 5) or persistent OSA (AHI ≥ 5) (77.5% SD 28.2 versus 65.8% SD 21.2; p = 0.204). Postoperative QoL scores and postoperative OSA evaluation are displayed in Table 3.

Table 3 - Postoperative IWQoL-Lite scores and postoperative OSA evaluation

Variable IWQoL-Lite	OSA remission versus persistent OSA (n=13 versus n=18)		
PF (SD)	97.0 (4.4)	82.8 (19.7)	p=0.008
SE (SD)	89.8 (19.1)	72.8 (27.7)	p=0.066
SL (SD)	90.9 (16.3)	79.9 (25.9)	p=0.187
PD (SD)	98.8 (3.0)	77.2 (28.4)	p=0.005
W (SD)	96.2 (6.5)	83.7 (25.8)	p=0.064
Total (SD)	94.8 (7.3)	79.4 (21.8)	p=0.011

OSA = Obstructive Sleep Apnea; PD = Public Distress; PF = Physical Functioning; Postop = Postoperative score; Preop = Preoperative score; SE = Self-Esteem; SL = Sexual Life; Total = Total score; W = Work

DISCUSSION

This study was the first QoL study that accurately diagnosed OSA by performing routine P(S)G measurements in all patients preoperatively. This study shows that OSA has no influence on preoperative QoL in bariatric surgery patients. After surgery, OSA patients showed significantly less improvement of Public Distress and Work. While these differences are minimal and probably without any clinical consequences, differences between patients with an AHI ≥ 30/hour and patients with an AHI < 5/hour are larger and therefore clinically more important during follow-up.

Furthermore, it remains challenging to conclude that OSA remission/persistence has an independent influence on the QoL. Although no significance level was reached, patients with OSA remission had more excess weight loss than patients with persistent OSA. As this discrepancy is probably caused by the small number of patients who repeated P(S)G after surgery, it would be interesting to evaluate this finding in larger cohort studies. If OSA patients achieve less weight loss after bariatric surgery, this might be a selective group requiring additional weight loss programs.

This illustrates that a limitation of this study is the loss to follow-up. The amount of QoL improvement could influence patients' decision to show or not show up for postoperative P(S)G and patients' clinical symptoms probably have introduced bias.

Considering future studies, the Functional Outcomes of Sleep Questionnaire, which has been used in research and clinical practice to measure the impact of daytime sleepiness on activities of daily living could be of interest in this specific group[22-23]. Secondly, CPAP compliance has a marked effect on QoL[24-25]. It could be hypothesized that the negative effect of OSA on QoL is even greater without compliant CPAP use. As many patients find the usage of CPAP burdensome, it would, therefore, be interesting to include CPAP compliance in future research.

CONCLUSION

Bariatric surgery leads to a remarkable improvement of the QoL. A trend is seen towards less improvement of the postoperative Public Distress and Work scores if OSA, especially the severe form, is present. Extensive postoperative follow-up and weight loss interventions might be necessary for OSA patients who stagnate in QoL improvement. Nevertheless, this study shows that despite the persistence of OSA in some patients, impairing Public Distress and Work subscales, the overall improvement of QoL is still significant in both OSA and non-OSA patients after bariatric surgery.

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Persistent moderate or severe obstructive sleep apnea after laparoscopic Roux-en-Y gastric bypass patients: which patients?

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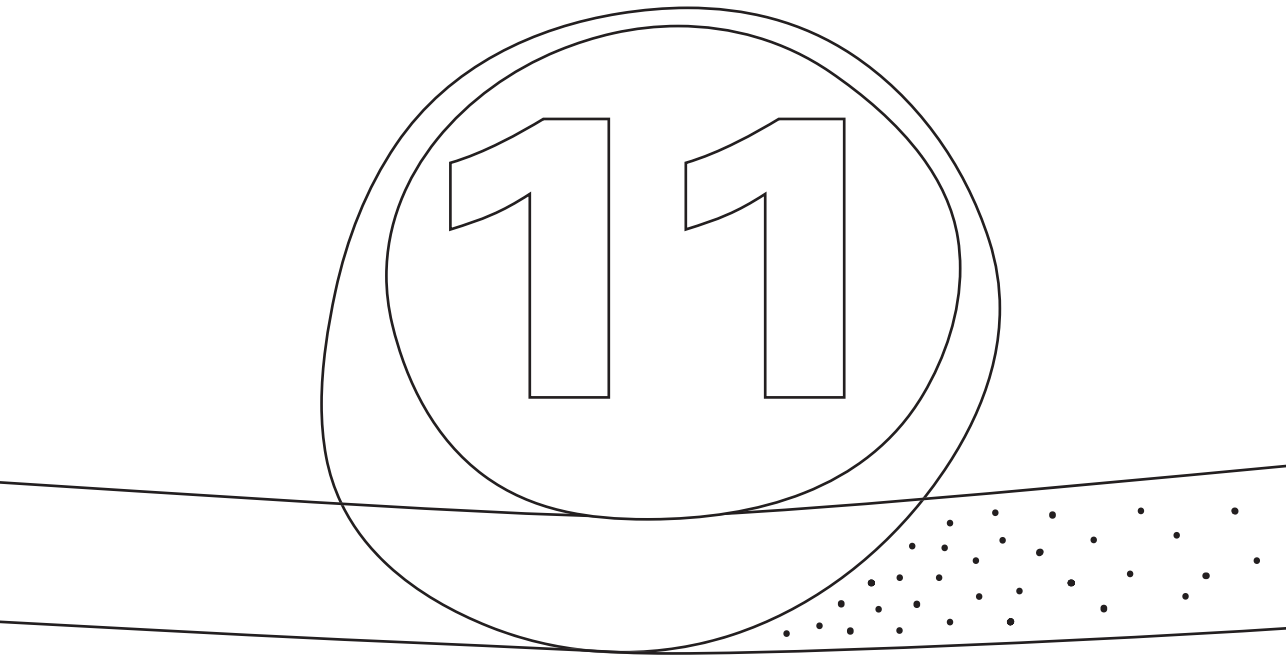

ABSTRACT

Introduction: Patients with severe obesity and obstructive sleep apnea (OSA) might decide to undergo bariatric surgery in order to improve this disease, or more specifically, to become independent of continuous positive airway pressure (CPAP) therapy, which is generally indicated in case of moderate and severe OSA. Knowledge of this topic is important for patient education on expectations of surgical outcome.

Objectives: To evaluate the prevalence and phenotypes of patients with persistent moderate to severe OSA after bariatric surgery.

Setting: Obesity Center Amsterdam, Amsterdam, the Netherlands.

Methods: Patients who underwent a laparoscopic Roux-en-Y gastric bypass, had a preoperative apnea-hypopnea-index (AHI) ≥ 15/hour and of whom a follow-up AHI was available were included.

Results: Out of 437 patients, 205 underwent pre- and postoperative poly(somno)graphy; 232 (53.1%) were lost to follow-up. Median AHI was 32.3/hour (range 15-138) and mean Body Mass Index 46 (standard deviation 7.2) kg/m^2. A postoperative AHI < 15/hour was achieved in 152 (74.1%) patients, whereas 53 (25.9%) still had moderate or severe disease, 8.6 (SD 4.8) months post-surgery. Predictive factors for persistent moderate to severe disease were age ≥ 50 years, preoperative AHI ≥ 30/hour, Excess Weight Loss (EWL) < 60% and hypertension (area under the curve: 0.772).

Conclusion: After bariatric surgery, around three-quarters of the moderate/severe OSA patients became non- or mild OSA patients, whereas a quarter (25.9%) still had moderate/severe OSA. Age ≥ 50 years, preoperative AHI ≥ 30/hour, EWL < 60% and hypertension were predictive factors for this persistent postoperative AHI ≥ 15/hour.

INTRODUCTION

Worldwide, there is an increase of the performance of bariatric surgery as a long-term treatment modality for morbid obesity[1]. Morbid obesity is well known for its association with type II diabetes and cardiovascular (CV) disease. In addition, obesity is an important risk factor for obstructive sleep apnea (OSA). These obesity associated comorbidities contribute to the decision to opt for bariatric surgery as a therapeutic method to control these diseases. Studies report that 60-70% of bariatric surgery patients suffer from OSA, which is generally associated with an increased CV and pulmonary risk in the perioperative period and on the long-term[2-3]. The gold standard to diagnose OSA is a poly(somno)graphy (P(S)G)[4]. The latter provides amongst other things, the apnea-hypopnea-index (AHI) used to indicate OSA severity. Continuous positive airway pressure (CPAP) is generally recommended for patients with an AHI ≥ 15/hour in order to treat both clinical symptoms and reduce long-term CV and pulmonary risk. In bariatric surgery, these patients are also treated with CPAP in the perioperative period in order to reduce the perioperative CV and pulmonary complication risk.

In approximately 75-80% of patients, bariatric surgery initiates dramatic improvement and even remission of clinical and sleep parameters in patients with OSA[5-6]. Nevertheless, some patients have residual disease despite weight loss following bariatric surgery[7-9]. In a cohort of 110 patients with a preoperative AHI ≥ 5/hour, patients with mild disease (AHI 5-15/hour) were more likely to have resolved OSA than those with severe (AHI ≥ 30/hour) OSA (53.6% vs. 17.9%)[9]. Additionally, approximately a third of patients undergoing bariatric surgery still suffer from moderate or severe disease[9]. These patients need continued treatment for OSA and often remain CPAP dependent. Although the gross majority of patients will report a significant decrease in AHI and other OSA parameters, it is poorly understood which patients will benefit and it remains difficult to predict what the effect of bariatric surgery will be on sleep parameters. Although a higher preoperative Body Mass Index (BMI) is associated with greater reduction of the AHI after bariatric surgery, studies demonstrate absence of a linear relationship between the extent of weight loss and improvement in OSA[9-12]. This complicates patient education on expectations of surgical outcome.

Bearing this in mind, we aim to evaluate the prevalence and phenotypes of patients with persistent moderate to severe OSA and therefore hypothetically CPAP dependency after bariatric surgery.

METHODS

Study design and study population

We performed a retrospective chart review of a consecutive series of patients who underwent a primary laparoscopic Roux-en-Y gastric bypass (LRYGB) in the period 2008–2015. As this study aims to investigate the reduction in AHI of moderate to severe OSA, patients were included in the study if the following inclusion criteria were met a) a preoperative AHI ≥ 15/hour, as measured by P(S)G in our clinic and b) a postoperative P(S)G in our clinic. Patients with a preoperative AHI < 15/hour and patients who did not undergo a postoperative P(S)G, despite a preoperative AHI ≥ 15/hour were excluded from analysis. Other surgical procedures were not included in order to avoid bias; as the type of surgical procedure influences weight loss, different weight loss outcomes consequently result in different AHI improvement.

All patients, who underwent bariatric surgery for morbid obesity in the Obesity Center Amsterdam, fulfilled the criteria for bariatric surgery of the International Federation for the Surgery of Obesity and metabolic disorders (IFSO). Baseline characteristics, including gender, BMI, waist circumference, comorbidities and intoxications, were collected from patient medical records. The local Institutional Review Board provided approval for this study.

Poly(somno)graphy

Since 2012, all patients scheduled for bariatric surgery undergo a mandatory preoperative P(S)G. Besides patients with OSA previously diagnosed elsewhere, all patients underwent a full-night comprehensive sleep study (PSG) using a digital Embla recorder (Flaga Medical devices, Reykjavik, Iceland). This records sleep architecture (derived from electroencephalogram, electrooculogram, and submental electromyogram), respiration (thoracic and abdominal measurement), movements of limbs, body position (trunk measurement), nasal airflow, and the intensity of the snoring (the last two measured by a pressure sensor). Pulse oximetry was used to monitor oxygen saturation (SaO2) and heart rate. Due to financial and capacity restrictions, a percentage of patients underwent a home PG using a digital Embla titanium recorder (Flaga Medical devices, Reykjavik, Iceland) instead of a PSG (44.9% preoperatively; 31.2% postoperatively). The same parameters are recorded except for the sleep architecture.

CPAP was prescribed in most patients with an AHI ≥ 15/hour. Six to nine months after surgery, all patients with a preoperative AHI ≥ 15/hour were invited for a second P(S)G, after which was decided whether patients still required CPAP therapy.

Definitions

The severity of OSA is expressed in the AHI. Obstructive apneas were defined as cessation of airflow for at least 10 seconds. Hypopneas were defined as periods of reduction of 30% oronasal airflow for at least 10 seconds and a 4% decrease in oxygen saturation. Arousals were not scored as hypopneas. The AHI was calculated

as the sum of total events (apneas and hypopneas) per hour of sleep. An AHI of 5–15/hour is mild OSA, an AHI of 15–30/hour is moderate and AHI of 30/hour is severe OSA, as assessed by PSG.

Excess weight loss (EWL) was calculated by using a BMI of 25 kg/m^2 as ideal body weight.

Surgical procedure LRYGB

All LRYGB procedures were performed according to a standardized technique which was already described in a previous article[14].

Data collection and statistical analysis

All data were collected from patient medical records and were anonymously entered in a database. Collected baseline variables were gender, age, AHI, BMI, waist circumference, type II diabetes, hypertension and dyslipidemia. These variables were chosen as increasing AHI thresholds go along with increased prevalence of male gender, higher age, BMI and waist circumference and increasing prevalence of hypertension, type II diabetes and dyslipidemia. The distribution of recorded variables was characterized by calculating the mean and standard deviation or in case of non-normal distribution (as shown by histogram) median and range.

Patients were subdivided into two study groups: postoperative AHI < or ≥ 15/hour. Continuous data were compared using the independent t-test or Mann-Whitney U test and categorical variables using the Chi-square test. Next to this, the percentage of patients with a postoperative AHI lower than 15/hour after surgery will be calculated for other preoperative AHI cut-off points, including 30/hour, 60/hour and 90/hour.

Additionally, the actual postoperative CPAP advice of patients' pulmonologist/otolaryngologist was collected. This was done as some patients are advised to continue CPAP therapy for a longer period despite an AHI lower than 15/hour. Reasons for this decision are clinical symptoms and persistent accompanying comorbidities. Finally, a multivariable prediction model was developed for persistent postoperative AHI greater than 15/hour after bariatric surgery. This was established with logistic regression analysis according to the TRIPOD statement[15]. As the continuous variables were not linear with the outcome, these variables were dichotomized. Age and EWL were divided in two equal groups (younger/older than 50 years and higher or lower EWL than 60%). The AHI cut-off point was 30/hour, which is the cut-off point between moderate and severe OSA. Finally, a ROC-curve provided the area under the curve (AUC).

RESULTS

Study population

Two hundred and five patients were included in this study. **Figure 1** represents a flow-diagram of the patients excluded from this study. A total of 232 (53.1%) were lost to follow-up. Patient characteristics are shown in **Table 1** for both the total study population and subdivided in two groups: post-operative AHI < or ≥ 15/hour. The total study population consisted of 130 (63.4%) women and 75 (36.6%) men. At time of surgery, mean age was 48.8 years (9.3), median AHI 32.3/hour (range 15-138) and mean BMI 46 kg/m^2 (7.2). Based on the preoperative P(S)G results, 94 (45.9%) patients were diagnosed with moderate OSA and 111 (54.1%) patients with severe OSA. Of the 205 patients with a preoperative AHI greater than 15/hour, 194 patients (94.6%) received CPAP therapy, whereas no CPAP was prescribed in 11 patients (5.4%) as a decrease was expected after bariatric surgery.

Table 1 - Comparison of preoperative baseline characteristics between patients with and without persistent CPAP therapy 8.6 months after bariatric surgery

Variable	All patients (n=205)	No CPAP indication after surgery (n=152)	Persistent indication after surgery (n=53)	p value
Gender; n (%)				< 0.01[2]
Female	130 (63.4)	105 (69.1)	25 (47.2)	
Male	75 (36.6)	47 (30.9)	28 (52.8)	
Age; years (SD)	48.8 (9.3)	47.9 (9.6)	51.3 (7.8)	< 0.01[1]
AHI (range)	32.3 (15-138)	27 (15-104)	56 (15-138)	< 0.01[3]
BMI; kg/m² (SD)	46 (7.2)	45.7 (7.3)	46.9 (6.8)	0.279[1]
Waist circumference; cm (SD) (n=181)	134.1 (15.8)	132.6 (15.8)	138.7 (17)	0.022[1]
Type II diabetes; n (%)	86 (42)	62 (40.8)	24 (45.3)	0.568[2]
Hypertension; n (%)	118 (57.6)	81 (53.3)	37 (69.8)	0.036[2]
Dyslipidemia; n (%)	61 (29.8)	41 (27)	20 (37.7)	0.140[2]

AHI = Apnea Hypopnea Index; BMI = Body Mass Index; CPAP = Continuous Positive Airway Pressure; SD = Standard Deviation

[1] Independent t-test; [2] Chi-square test; [3] Mann-Whitney U test

Postoperative results

As shown in **Table 2**, after a mean follow-up of 8.6 (4.8) months, the median AHI of the total study population decreased from 32.3/hour (range 15-138) to 8.5/ hour (range 0-53.6).

Four out of 205 patients (2%) experienced a postoperative cardiopulmonary/neurovascular complication. One patient developed pneumonia, one patient developed respiratory insufficiency due to COPD exacerbation, two patients developed atrial fibrillation, of which one patient was already known with atrial fibrillation in medical

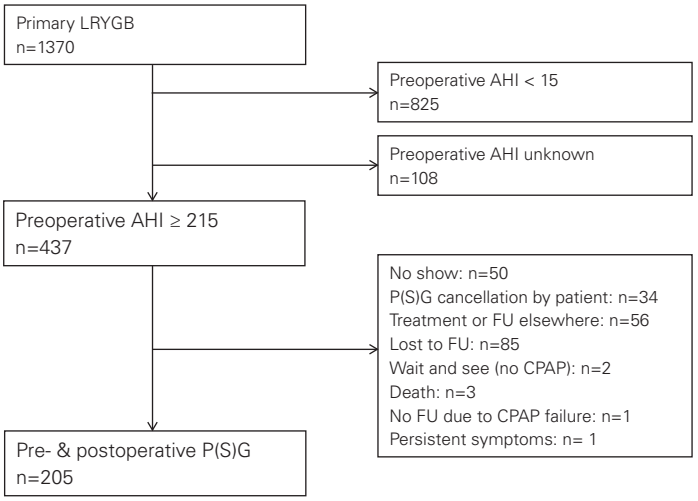

Figure 1 - Flowchart study population
AHI = Apnea-hypopnea-index; CPAP = Continuous Positive Airway Pressure; FU = Follow-up; LRYGB = Laparoscopic Roux-en-Y gastric bypass; P(S)G = Poly(somno)graphy

history. None of the 11 patients without CPAP developed a postoperative cardiopulmonary/neurovascular complication.

Mean total body weight decreased from 134 (28) kg to 98 (21) kg, equaling to a mean total weight loss (TWL) of 36 (13) kg and 26.4% (6.7) TWL. The mean BMI decreased from 46 (7.2) to 33.7 (5.5), leading to mean BMI loss of 12.2 (4) and mean EWL of 61.1% (17.9).

Table 2 - Postoperative results of patients with and without persistent CPAP therapy, 8.6 months after bariatric surgery

Variable	All patients (n=205)	No CPAP indication after surgery (n=152)	Persistent indication after surgery (n=53)	p value
Mean follow-up; months (SD)	8.6 (4.8)	8.7 (5.2)	8.3 (3.6)	0.604[1]
Postoperative AHI; per hour (range)	8.5 (0-53.6)	5.8 (0-14.8)	23.4 (15-53.6)	< 0.01[2]
Postoperative BMI; kg/m² (SD)	33.7 (5.5)	33.3 (5.5)	35 (5.4)	0.052[1]
Mean TWL; kg (SD)	35.8 (12.8)	35.9 (12.7)	35.3 (13.3)	0.636[1]
Mean BMI loss; kg/m² (SD)	12.2 (4)	12.4 (3.9)	11.9 (4.2)	0.434[1]
Postoperative EWL; % (SD)	61.1 (17.9)	62.8 (17.4)	56.3 (18.8)	0.023[1]

AHI = Apnea-hypopnea-index; BMI = Body mass Index; CPAP = Continuous Positive Airway Pressure; EWL = Excess Weight Loss; TWL = Total Weight Loss; SD = Standard Deviation; [1] Independent t-test; [2] Mann-Whitney U test

Subdivision postoperative AHI < or ≥ 15/hour

A total of 8.6 (4.8) months after surgery, 152 (74.1%) had an AHI < 15/hour. Comparing the preoperative data between the patients with a postoperative AHI < and ≥ 15/hour, the latter were statistically significantly older, had a higher preoperative AHI/hour and waist circumference, a higher incidence of hypertension and had a greater percentage of males (see **Table 1**). The majority (90.4%) of moderate OSA patients (AHI 15-30/hour) achieved a postoperative AHI below 15/hour after surgery. Of the patients with a preoperative AHI of 30-60/hour, 60-90/hour and > 90/hour, a total of 45 (70.3%), 21 (56.8%) and 1 (10%) patients respectively, achieved an AHI level below 15/hour post-surgery (**Figure 2**).

Fifty-three (25.9%) patients with a postoperative AHI ≥ 15/hour had a postoperative median AHI of 23.4/hour (range 15-53.6). Within this group (n=53), 38 (71.7%) and 15 (28.3%) had moderate and severe OSA respectively. Postoperative EWL was lower in the group with persistent moderate to severe OSA in comparison with those becoming non- or mild OSA patients (56.3 ±18.8 versus 62.8 ±17.4; p=0.023). The mean decrease in total weight loss in kg and BMI was not different between the two groups.

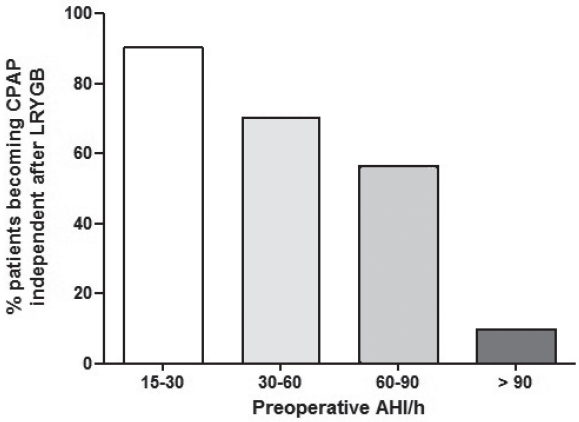

Figure 2 - Percentage of moderate to severe OSA patients in who CPAP is no longer necessary 8.6 months after bariatric surgery
AHI = Apnea-hypopnea-index; CPAP = Continuous Positive Airway Pressure; LRYGB = Laparoscopic Roux-en-Y gastric bypass

CPAP therapy after surgery

A total of 131 patients (63.9%) no longer required no CPAP according to their pulmonologist/otolaryngologist, whereas 54 patients (26.3%) were advised to continue CPAP until a second postoperative P(S)G. No documentation about CPAP prescription was found in 20 mild OSA (AHI 5-15) patients (9.8%). Thirteen out of 152 patients

with a postoperative AHI < 15/hour continued CPAP therapy and were invited for second postoperative P(S)G after more weight loss achievement.

Of the 54 patients with persistent CPAP indication after first follow-up, a second postoperative P(S)G was performed in 21 patients (38.9%). Of these 21 patients, the median AHI decreased from 21.7 (IQR 17.8) to 13 (IQR 15.2). Five no longer required CPAP, 10 patients were advised to continue CPAP and no documentation about CPAP was found for 6 patients. All patients with persistent CPAP dependency and/or without second P(S)G are still treated by their pulmonologist/otolaryngologist.

Predictive factors for persistent CPAP indication after bariatric surgery

Although a significant correlation was found between postoperative AHI and %EWL (-0.212, $p < 0.01$), no linear relationship could be detected in current cohort as seen in a scatter plot. The %EWL was therefore divided in two equal groups that resulted in a cut-off point of 61.1%. As 60-80% EWL is mostly achieved after bypass surgery, 60% EWL was used as cut-off point for this study. Sixty percent EWL was more often achieved in patients with a postoperative AHI < 15/hour than patients with a persistent AHI ≥ 15/hour (54.6% versus 35.8%, $p = 0.019$).

On univariate analysis, male gender, age ≥ 50 years, preoperative AHI ≥ 30/hour, EWL < 60%, preoperative waist circumference ≥ 135 cm and hypertension were independent predictors for CPAP dependency ($p < 0.1$). Results are displayed in **Table 3**.

The most optimal multivariable prediction model included variables age ≥ 50 years, preoperative AHI ≥ 30/hour, EWL < 60% and preoperative hypertension (Nagelkerke 0.237; AUC 0.770). The multivariable prediction equation and the ROC-curve are showed in **Table 4** and **Figure 3** respectively.

Table 3 - Univariate logistic regression analysis – Predictors for persistent CPAP dependency after bariatric surgery

	Persistent CPAP dependency after bariatric surgery		
Variable	OR	95% CI	p value*
Male gender	2.502	1.320-4.744	< 0.01
Age > 50 years	2.278	1.187-4.371	0.013
Preoperative AHI > 30/hour	6.202	2.828-13.602	< 0.01
EWL < 60%	2.127	1.114-4.059	0.022
Preoperative WC > 135cm	1.853	0.929-3.695	0.080
Type II diabetes	1.201	0.640-2.256	0.568
Hypertension	2.027	1.040-3.951	0.038
Dyslipidemia	1.641	0.847-3.177	0.142
Alcohol	0.950	0.491-1.838	0.879
Smoking	1.010	0.420-2.430	0.982

AHI = Apnea Hypopnea index; BMI = Body Mass Index; C.I. = Confidence Interval; CPAP = Continuous Positive Airway Pressure; WC = Waist Circumference

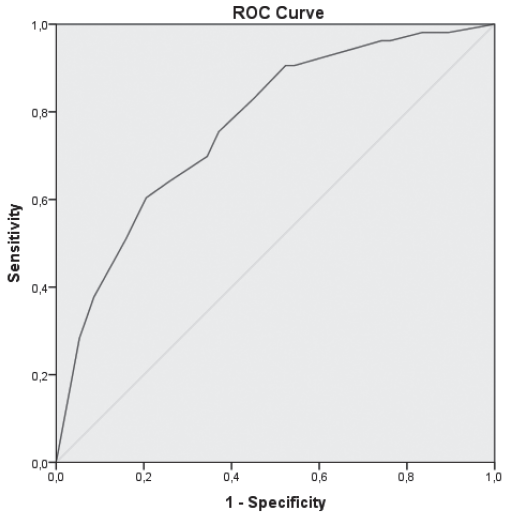

Figure 3 - ROC curve multivariable prediction model
Area under de curve: 0.770; Standard Error: 0.037
95% Confidence Interval: 0.698-0.841; p < 0.01

Table 4 - Multivariable logistic regression analysis; predictors for persistent CPAP dependency after bariatric surgery

	Persistent CPAP dependency after bariatric surgery		
Variable	OR	95% CI	p value*
Age > 50 years	2.146	0.944-4.880	0.068
Preoperative AHI > 30/hour	5.679	2.436-13.237	< 0.01
EWL < 60%	2.137	1.002-4.556	0.049
Hypertension	1.854	0.804-4.272	0.147
Constant	0.034		< 0.01

AHI = Apnea Hypopnea index; C.I. = Confidence Interval; CPAP = Continuous Positive Airway Pressure; OR = Odds ratio
*Hosmer and Lemeshow test: p = 0.792; Nagelkerke R square: 0.247

DISCUSSION

To our best knowledge this is the largest cohort of patients undergoing bariatric surgery with both a pre- and postoperative P(S)G described in the literature. We report that almost three-quarter of moderate to severe OSA patients achieve a postoperative AHI below 15/hour after LRYGB surgery. However, more than a quarter (25.8%) of patients still have moderate to severe OSA after surgery. A relevant finding for nearly 35% (n=437) of patients who underwent a mandatory PSG before undergoing LRYGB in our center (see **Figure 1**). Only 9.6% with a preoperative AHI of 15-30/hour hypothetically still need CPAP after surgery. This is 29.7% in case of an AHI of 30-60/hour. On the other hand, only 56.8% with an AHI of 60-90/hour and 10% of an AHI > 90 decrease to an AHI below 15/hour after surgery. As a PG instead of a PSG might underestimate the AHI, it is likely that these percentages might even be higher[14].

An important limitation of this study is the loss to follow-up. A total of 232 (53.1%) patients did not undergo a postoperative P(S)G (see **Figure 1**). The majority of these patients (36.2%) did not show up or cancelled their appointment. The postoperative course of these patients might be relevant for current results. Their reason to avoid follow-up remains unclear. On the one hand, we may be underestimating the percentage of patients with a postoperative AHI < 15, since patients with residual symptoms may be keener for re-evaluation. It can be hypothesized that patients with resolution of symptoms, are more reluctant to undergo a burdensome P(S)G, while they may still suffer from residual disease, but less severe. On the other hand, patients who have not reached sufficient EWL may be discouraged to continue follow-up. A low compliance in both CPAP use and follow-up has previously been described in the bariatric literature, showing that around 40% of the bariatric surgery patients underwent a postoperative P(S)G and 70% are CPAP non-compliant[14;16].

This finding shows that there is a need for better follow-up strategies. Also, the required CPAP pressure is likely to reduce as the BMI/AHI decreases. Patients who remain CPAP dependent, but are not sufficiently treated might have an increased long-term CV and pulmonary risk and might also have an increased the risk of being involved in traffic accidents. Furthermore, clinical symptoms such as sleepiness might induce social problems i.e. personal and work problems and are easily to avoid with proper treatment.

Another interesting question is the period of time between discontinuing CPAP and follow-up P(S)G. A recently published study of Vroegop et al. showed that there is some evidence that so called CPAP wash-out exists[17]. A limitation of the current study population is that patients were not advised to discontinue CPAP before follow-up P(S)G.

Also, it is important to realize that patients, who are no longer CPAP dependent after bariatric surgery, might have become positional OSA (POSA) patients, who might benefit from therapy. Literature shows that around 50% of patients become POSA patients, meaning their AHI is at least twice as high in supine position than

in other positions[18]. Or in other words, severe non positional OSA can reverse to less severe positional OSA. Although therapy seems not necessary to prevent CV and pulmonary complications, CPAP or positional therapy might still be indicated in patients with clinical symptoms[19].

A previous study examined predictive factors for cure (AHI < 5) and found that age, preoperative BMI and weight in all combinations were inadequate predictors ($p > 0.05$)[9]. However, the chosen cut-off of 15/hour in this study resulted in the detection of predictive factors and are therefore recommended in the clinical setting.

Concerning persistent CPAP therapy after bariatric surgery, factors age, preoperative AHI, EWL and hypertension predict 23.7% of developing this outcome. Consequently, 76.3% is a result of other factors. BMI was not included in current multivariable model. While a higher preoperative BMI leads to less AHI improvement in literature, preoperative BMI was not different between both study groups. This could be a result of losing information by dividing patients in only two study groups and an overall BMI of 46 (7.2) kg/m^2. Performing these analyses in a group of super obese patients (BMI ≥ 50 kg/m^2) might be interesting for future research.

In addition, neck circumference was not included in current analysis due to missing data in the majority of the population. However, an association between neck circumference and AHI has been described in previous studies[2;20]. Moreover, the role of bicarbonate in the detection of OSA has not been investigated in the bariatric surgery population. However, baseline serum bicarbonate could be an important value to review in relation to the degree of decrease in AHI. Therefore, including these variables in the multivariable model might increase its predictive value and should therefore also be included in future studies.

A limitation of this study is the loss of information in the multivariable model by dichotomizing the preoperative AHI. Although a continuous scale of the preoperative AHI is preferred, the relationship of the variable and the probability of the outcome were not linear and therefore not included. Secondly, the preoperative AHI was categorized in four groups as displayed in **Figure 2**. However, the 95% confidence interval of the AHI ≥ 90/hour was unacceptable large due to the small number of patients included in this group. Therefore, a dichotomized variable was chosen as most useful variable within this study. Moreover, preoperative hypertension appeared to be a predictive value. However, this was regardless of resolution postoperatively. It would be interesting for further research to investigate whether improved or resolved hypertension is associated with a postoperative AHI < 15/hour.

Finally, the percentage of EWL was significantly less in patients with persistent moderate to severe OSA after surgery (56.3% (18.8) versus 62.8% (17.4); $p = 0.023$). Nevertheless, the clinical value is probably low as the preoperative BMI (overall 46 SD 7.2), total body weight loss and BMI loss was comparable between groups. This might be a consequence of a relative short follow-up after surgery i.e. 8.6 (4.8) months. Further decrease of the AHI is expected after increased weight loss in the

long term. As there is no literature available regarding the optimal postoperative timing for follow-up P(S)G, this would be an interesting question for future studies.

Finally, although no linear relationship was found between postoperative AHI and %EWL, a difference in weight loss was seen between patients with an AHI < or ≥ 15/hour and EWL < or ≥ 60%. This discrepancy is probably caused by dichotomizing both variables and therefore losing much (continuous) data. Although current and published study results show that there is some relationship between weight loss and OSA improvement, physicians should bear this in mind when predicting postoperative AHI after weight loss.

CONCLUSION

OSA is one of the most common comorbidities among morbidly obese patients. This study shows that almost three-quarter of the moderate to severe OSA patients achieve a postoperative AHI below 15/hour and hypothetically no longer require CPAP therapy after LRYGB. Yet, a quarter (25.8%) still has moderate/severe OSA after surgery. Predictive factors for this persistent disease are age ≥ 50 years, preoperative AHI ≥ 30/hour, EWL < 60% and hypertension. This result is essential in informing morbidly obese patients prior to bariatric surgery, especially for those who deliberately seek surgery as a solution for both their OSA and morbid obesity. Furthermore, this knowledge allows physicians to provide targeted follow-up.

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Perioperative care of obstructive sleep apnea in bariatric surgery: a consensus based guideline

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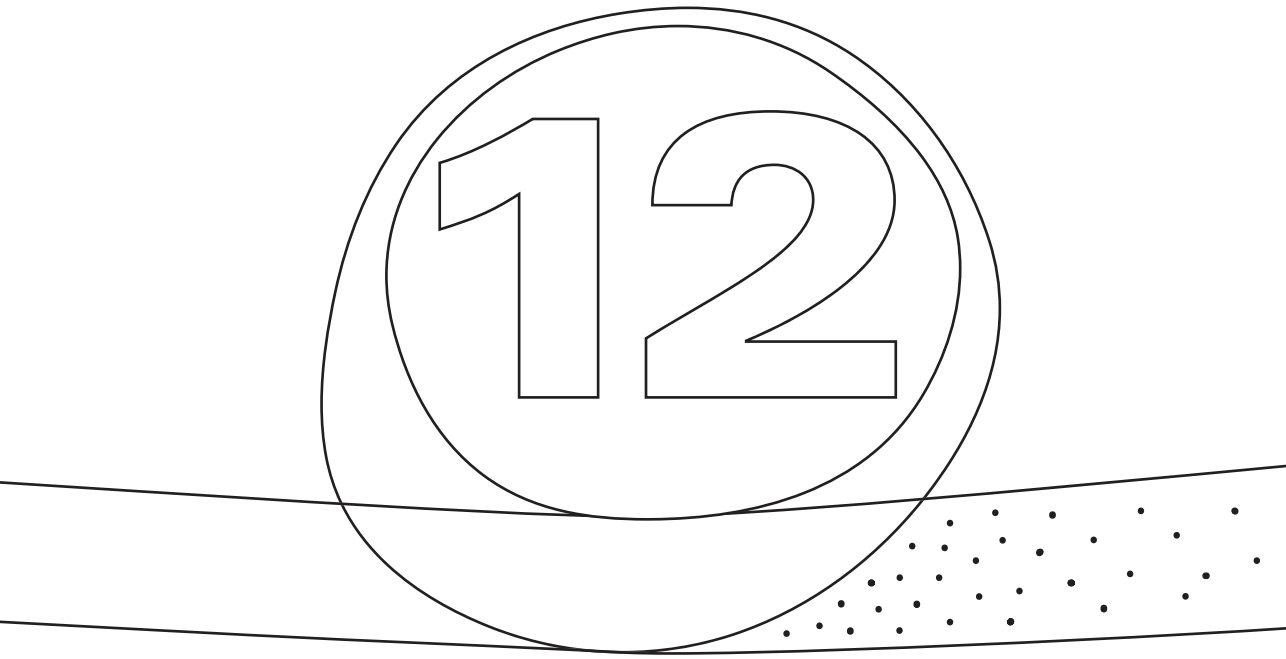

ABSTRACT

Introduction: The frequency of bariatric surgery is increasing worldwide, with over 500,000 cases performed every year. Obstructive sleep apnea (OSA) is present in 35%-94% of bariatric patients. Nevertheless, consensus regarding the perioperative management of OSA in bariatric surgery patients is not established.

Objectives: To provide consensus based guidelines utilizing current literature and, when in the absence of supporting clinical data, expert opinion by organizing a consensus meeting of experts from relevant specialties.

Setting: The meeting was held in Amsterdam, the Netherlands.

Methods: A panel of 15 international experts identified 75 questions covering preoperative screening, treatment, postoperative monitoring, anesthetic care and follow-up. Six researchers reviewed the literature systematically. During this meeting, the "Amsterdam Delphi Method" was utilized including controlled acquisition of feedback, aggregation of responses and iteration.

Results: Recommendations or statements were provided for 58 questions. In the judgement of the experts, seventeen questions provided no additional useful information and it was agreed to exclude them. With the exception of three recommendations (64%, 66% and 66% respectively), consensus (> 70%) was reached for 55 statements and recommendations. Several highlights: polysomnography is the gold standard for diagnosing OSA; continuous positive airway pressure is recommended for all patients with moderate and severe OSA; OSA patients should be continuously monitored with pulse oximetry in the early postoperative period; perioperative usage of sedatives and opioids should be minimized.

Conclusion: This first international expert meeting provided 58 statements and recommendations for a clinical consensus guideline regarding the perioperative management of OSA patients undergoing bariatric surgery.

INTRODUCTION

Bariatric surgery is increasingly being performed as a long-term treatment for morbid obesity, which is defined as a Body Mass Index (BMI) greater than 40 kg/m^2 or as a BMI greater than 35 kg/m^2 in combination with obesity related comorbidities. Current bariatric practice supports extending the BMI limit down to 30 for certain comorbid conditions such as type II diabetes. At present, around 500,000 bariatric procedures are performed worldwide and the number is growing[1]. Morbid obesity is associated with multiple comorbidities, of which one of the most common is obstructive sleep apnea (OSA). Numerous articles showing a dramatic decrease in OSA severity after surgically induced weight loss have been published. Nevertheless, one must not forget that unrecognized and untreated OSA is characterized by repetitive collapses of the upper airway leading to intermittent hypoxia, sympathetic activation and, with obesity, increased carbon dioxide levels. Due to these pathophysiological changes, there is an increased risk of cardiovascular, neurovascular and pulmonary comorbidities. These include systemic and/or pulmonary hypertension, coronary artery disease, atrial fibrillation, cerebral vascular accidents and type II diabetes.

Two meta-analyses and a recent systematic review of 63 publications reporting 413,576 OSA patients and 8,557,044 control (non-OSA) patients confirmed a higher incidence of postoperative oxygen desaturations, cardiac events and respiratory failure in the presence of OSA[2-5]. Postoperative respiratory complications in patients with OSA include hypoxia, hypercapnia, pneumonia, atelectasis, bronchospasm, acute respiratory distress syndrome, pulmonary edema and the need for non-invasive and/or reintubation. Reported cardiovascular complications are arrhythmia, myocardial ischemia and pulmonary embolism; central nervous system complications are delirium, encephalopathy and apoplexia; other organ system complications are acute renal failure, gastrointestinal bleeding and wound hematoma. Another important comorbidity includes obesity hypoventilation syndrome (OHS) which clearly increases morbidity and mortality and is often associated with severe obesity and OSA. These patients have a markedly decreased expiratory reserve volume. Unexpected complications often result in unscheduled transfer to a higher care level and increased duration of hospital stay.

While independent guidelines were available for both bariatric surgery and OSA management, no guideline has been available that addresses both issues despite the high prevalence (35%-93.6%) of OSA in the bariatric population[6-19]. As OSA and morbid obesity are independently associated with an increased perioperative risk, preparing guidelines addressing these patients' perioperative care requires a multidisciplinary approach. With a multidisciplinary panel of experts whose expertise covered the continuum of care of these patients, all relevant aspects of perioperative care will extensively be addressed. Our aim was to provide consensus based guidelines for this topic. This was done by using current literature and, in the absence of supporting clinical data, expert opinion. For these matters, a consensus meeting was held with experts from the relevant specialties.

METHODS

Group and main topics

Five authors were involved in the organization of this project (CdR, MGS, NdV, AS and BvW). A multidisciplinary panel of 15 international experts was invited to attend a consensus meeting held in Amsterdam of March 2016. The selection of panelists was based on the extensive clinical experience of experts in the field of sleep, anesthesiology, pulmonology, otorhinolaryngology & head and neck surgery, bariatric surgery and clinical neurophysiology. Additionally, the Executive Board of the International Federation for the Surgery of Obesity and Metabolic disorders (IFSO) was asked to provide suggestions for experts within their network.

This consensus meeting was held under the principles established for the 2015 consensus meeting on appendicitis of the European Association for Endoscopic Surgery (EAES)[20]. Accordingly, the head of experts of the EAES meeting (HJB) operated as an external advisor prior to and during the current meeting. Furthermore, the meeting included two independent moderators (CdR and MGS), six researchers (BR, MT, NvdW, UC, AvR, RvdH) and one independent information specialist (RS).

The organizing group identified five main topics in which there remains lack of consensus. These five topics include: 1) preoperative screening; 2) treatment; 3) postoperative monitoring; 4) anesthetic care and 5) follow-up of OSA patients undergoing bariatric surgery. Consequently, all experts were approached and asked to provide clinically relevant questions within these topics before the meeting was held. The PICO format was used for framing the study questions when applicable. All experts provided approval for the final selection of study questions (**Appendix #1**).

Processing literature

An independent information specialist performed a systematic literature search on each main topic (**Supplementary Material #1**). Studies were identified by searching PubMed, Embase and the Cochrane Central Register for Controlled Trials. The last search was run on 07-12-2015. Studies were identified by using keywords "Bariatric Surgery" AND "Obstructive Sleep Apnea" AND "[subquestion]". In order to identify additional articles concerning morbidly obese patients, an additional search was performed by using keywords "Morbid Obesity" AND "Obstructive Sleep Apnea" AND "[subquestion]". Mesh terms and free text words were combined for both searches.

The articles were assembled in five separate Reference Manager (®) databases after which duplicates were removed. These five databases each covered one main topic. They were transmitted to the researchers for further selection.

The six researchers were divided into three teams of two members each. Each team received one or two databases. Both members of each team individually reviewed the same literature. Only articles written in English were included. Articles were selected based on their titles and abstracts. The remaining articles were read in full text and categorized according to subquestions developed for each topic. This

was followed by deliberation between team members regarding their suitability for inclusion in the analysis. In case of a lack of consensus between the researchers, two independent referees were available (CdR and MGS).

All categories of studies i.e. randomized controlled trials, retrospective studies and expert opinion, were eligible for inclusion. Level of evidence was provided for all articles according to the Oxford system[21]. During the process, team meetings were organized in order to assure that everyone followed the same strategy and to discuss any difficulties. A definitive list of full-text articles was transferred to the website Mendeley (®) where all articles were available online for the researchers and experts.

For each subquestion, the researchers prepared a preliminary answer based on the available literature. The answers included conclusions, recommendations, level of evidence of all included articles and strength of recommendations, according to the GRADE system[22]. Final grade for the quality of evidence was assigned as 'high' (⊠⊠⊠⊠) , 'moderate' (⊠⊠⊠□) , 'low' (⊠⊠□□) or 'very low' (⊠□□□) . Subsequently, all subquestions were distributed among all 15 experts based on their expertise. Experts were asked to review the literature and answers provided by the research teams and offer suggestions for correction using the experience and knowledge they have in the field. When no literature was available to answer a subquestion, the assigned expert was asked to provide an expert opinion.

Throughout the manuscript, recommendations or statements are referred to their main topic and subquestion. For example, topic 1 (preoperative screening) and subquestion 1 (prevalence of OSA in bariatric surgery) is documented as (Q 1.1). Results of every subquestion are displayed in **Table 1-5**.

Consensus Meeting

The consensus meeting was held on 17 and 18 March 2016 in Amsterdam, the Netherlands. All invited experts attended the meeting in person. The consensus meeting was held according to an adjusted Delphi methodology referred as to the "Amsterdam Delphi Method" in order to address the large number of questions[20]. The following key components of the Delphi method were used: iteration (two rounds); controlled acquisition of feedback and aggregation of responses. Anonymity, which is also a key component in the Delphi method, was not feasible in this face-to-face setting. 'Consensus' level was set at 70% agreement among experts[20]. This cut-off was validated and accepted in methods developed for the 2015 EAES consensus meeting on appendicitis[20]. The structure of the meeting is displayed in **Figure 1**. The two moderators independently chaired the meeting and kept time and track of the methodology.

When more appropriate, the experts could suggest a statement rather than a recommendation. Finally, in the judgment of the experts, questions were excluded from further process if they provided no additional useful information.

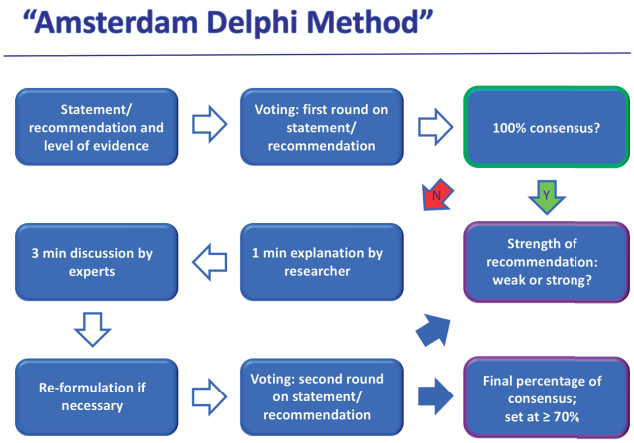

Figure 1 - Consensus meeting according to the "Amsterdam Delphi Method"

RESULTS

Literature search

Initially the searches were categorized as either focused on bariatric surgery or on morbid obesity. The "Bariatric Surgery" search resulted in 5546 articles. After duplicates were removed, a total of 2471 unique articles remained. An additional "Morbid Obesity" search provided 14,584 articles, of which 4882 articles remained after removing duplicates within this search and from the "Bariatric Surgery" search. Consequently, a total of 7353 articles were screened on title and abstract by our research teams. The selection procedure for each topic is displayed in **Figure 2**.

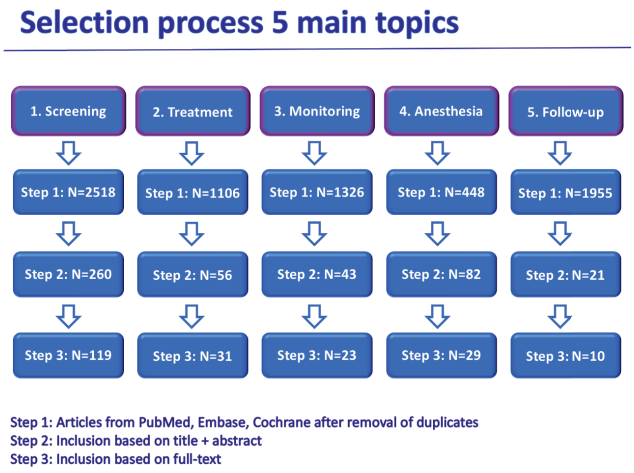

Figure 2 – Flowchart article selection

Consensus meeting

During the consensus meeting, all 75 study questions were addressed. Recommendations including their strength were provided for 49 questions. Nine questions resulted in the formulation of a clear statement, not requiring strength, instead of a recommendation. Seventeen questions provided no additional useful information and were voted out by the experts and thus excluded from being processed further. With the exception of three recommendations (64%, 66%, 66% respectively), consensus was reached for 55 statements and recommendations. Recommendations or statements, quality of evidence and strength of recommendations are displayed in **Tables 1-5**. Results of both voting rounds are shown in **Supplementary Material #2**.

Preoperative screening (Table 1)

The value of mandatory OSA screening in the preoperative period was one of the most important discussions held at the meeting.

OSA is one of the most common comorbidities among morbidly obese patients. Fourteen prospective studies were found that primarily investigated the prevalence of OSA using sleep studies. The prevalence varied between 35% and 94% (**Table 1**, Q 1.1)[6-19]. Of these 14 studies, 11 reported prevalence higher than 60%.

In general, adequate detection and treatment of OSA is important for three main reasons: reducing clinical symptoms such as sleepiness and cognitive dysfunction, reducing the long term cardio- and neurovascular risks and reducing the occurrence of traffic, domestic or workplace accidents. In morbidly obese patients requiring

Table 1 – Recommendations and statements concerning OSA preoperative screening in bariatric surgery

Question	Recommendation	% consensus	Quality of evidence	Strength of recommendation
1.1	The prevalence of OSA in bariatric surgery patients varies between 35% and 94%	-	⊠⊠⊠⊠	Statement
1.2	Clinically relevant perioperative complications seem more frequent in OSA patients	93	⊠□□□	Statement
1.3	CV, neuromuscular, and pulmonary outcomes are improved after bariatric surgery and this may be related to treatment of OSA	100	⊠□□□	Statement
1.4	CPAP is advisable to reduce the incidence of perioperative complications and CV risks	64*	⊠□□□	Weak
1.5	The gold standard for diagnosis of OSA is an overnight laboratory polysomnography	86	⊠⊠⊠⊠	Strong
1.6	Type 3 polygraphy can be used to screen for OSA in the bariatric population with high pre-test probability; its use is most reliable when moderately severe OSA is suspected	100	⊠⊠□□	Strong
1.7	The STOP-Bang score can be used as a screening tool to stratify high risk OSA	93	⊠⊠⊠□	Strong
1.8	The ESS should not be used as a screening tool for OSA	100	⊠⊠□□	Strong
1.9	The Berlin questionnaire can be used to stratify risk of OSA	93	⊠□□□	Weak
1.12	A portable monitor is a useful adjunct to questionnaires in OSA screening	100	⊠⊠⊠□	Weak

Table 1 – Recommendations and statements concerning OSA preoperative screening in bariatric surgery (continued)

Question	Recommendation	% consensus	Quality of evidence	Strength of recommendation
1.14	$PaCO_2$ does not indicate the risk of OSA; however, elevated $PaCO_2$ is important for perioperative risk stratification and is a diagnostic tool for OHS in a patient with OSA	100	☒☐☐☐	Strong
1.15	CO_2 measurements assessing the relation of OSA with perioperative complications should be implemented in future prospective trials to evaluate its role in risk stratification	100	☒☐☐☐	Statement
1.16	Venous $HCO3^-$ should be part of the routine screening tool for coexistence of OHS	100	☒☒☒☒	Strong
1.17	The ODI is a useful non-invasive severity measure; other measures need further evaluation	80	☒☒☒☐	Statement
1.18	OHS should be screened for in bariatric surgery patients with OSA (coexistence 20%)	100	☒☒☒☒	Strong
1.19	More research is needed to evaluate and introduce additional AHI cutoffs i.e. ≥ 60hour	80	☒☐☐☐	Statement
1.20	Length of operation, open or laparoscopic approach and level of expertise of a center may be of influence on OSA related outcome	93	☒☐☐☐	Weak
1.21	The presence of neuromuscular disorders or obstructive lung diseases should be considered as this might increase the perioperative risk of hypoventilation and upper airway obstruction	100	☒☒☐☐	Strong
1.22	There is no evidence that patients should specifically be investigated for VTE risk, unless they have a history of prior deep VTE and/or coagulation disorders	100	☒☐☐☐	Weak
1.23	The ODI seems reliable and clinically useful in detection OSA	93	☒☒☒☐	Strong

* Consensus level < 70%; Question 1.10, 1.11 and 1.13 were excluded

AHI = Apnea Hypopnea Index; CPAP = Continuous Positive Airway Pressure; CV = Cardiovascular ESS = Epworth Sleepiness Scale; ODI = Oxygen Desaturation Index; OHS = Obesity Hypoventilation Syndrome; OSA = Obstructive Sleep Apnea; VTE = Venous Thromboembolisms

general anesthesia, a fourth important reason is reducing the preventable perioperative risks, as clinically relevant complications seem more frequent in OSA patients (Table 1, Q 1.2)[23-40].

In the long term, cardiovascular, neurovascular and pulmonary outcomes are improved after bariatric surgery and this may be related to treatment of OSA through weight loss surgery (Table 1, Q 1.3). Considering perioperative complications in severely obese patients, adequate OSA treatment with Continuous Positive Airway Pressure (CPAP) is advisable to reduce the incidence of perioperative pulmonary complications and cardiovascular risks (Table 1, Q 1.4)[31;36;41]. In case of CPAP intolerance and/or low CPAP adherence, patients need to be considered for the most appropriate non-CPAP treatment option, such as oral appliances[42]. Other successful therapies include positional therapy, maxillofacial surgery and upper airway surgery/stimulation[43;44].

Currently, the gold standard for diagnosis of OSA is an overnight laboratory polysomnography (PSG) (Table 1, Q 1.5)[45-47]. Such a study determines the frequency and duration of apneas and hypopneas during a full night of accurately documented sleep and subsequently generates amongst other variables the apnea-hypopnea-index (AHI). Briefly, the AHI quantifies the number of pharyngeal collapses (partial or complete) per hour during sleep and is used to judge OSA severity. OSA is defined as an AHI ≥ 5/hour in adults. The internationally used severity levels are 5-14.9/hour (mild OSA), 15-29.9/hour (moderate OSA) and ≥ 30/hour (severe OSA). More research is needed to evaluate and introduce additional cutoffs, i.e. ≥ 60/hour to represent extremely severe OSA (Table 1, Q 1.19)[48].

Besides the AHI, there are other severity metrics available that could be considered. The oxygen desaturation index (ODI), which is also an accurate tool to screen for OSA (Table 1, Q 1.23)[49-56], has shown to be a useful non-invasive severity measure, whereas other measures such as length of apneas percentage of apneas and cumulated time for oxygen saturation < 90% need further evaluation (Table 1, Q. 1.17)[19;49;54;55;57-63]. One study found that patients with a mean preoperative overnight SpO2 <92.7% or ODI >28.5/hour or cumulative time percentage with SpO2 <90% more than >7.2% are at higher risk for postoperative adverse events[64].

A less time consuming and more patient friendly sleep study than PSG is a portable study of a limited range of variables, known as Type 3 portable sleep monitoring according to the definitions of the American Academy of Sleep Medicine[65]. This can be used to screen for OSA in the bariatric population with high pre-test probability. Its use is most reliable when moderate to severe OSA is suspected (Table 1, Q 1.6)[66;67].

Despite these findings regarding the value of overnight measurements to determine the perioperative risk, mandatory sleep studies prior to bariatric surgery have not been accepted as the standard of care due to limited sleep laboratory capacity, costs, time management and the often unknown importance of OSA detection. As a portable monitor is considered a useful adjunct to questionnaires in OSA screening (Table 1, Q 1.12)[68], this has led to the development of several other screening

questionnaires. A commonly used and validated questionnaire is the STOP-Bang, the score of which can be used as a screening tool to stratify high risk OSA in (morbidly) obese patients (**Table 1**, Q 1.7)[69]. This was also the conclusion in two more recent studies[70;71]. Additionally, with a sensitivity of 86% and specificity of 77%, the Berlin questionnaire can also be used to identify risk of OSA (**Table 1**, Q 1.9)[72-74]. The Epworth Sleepiness Scale, however, should not be used as a screening tool for OSA, as this is a symptom severity score and has a poor correlation in the bariatric population for OSA detection (**Table 1**, Q 1.8)[14;15;53;75].

In addition to screening questionnaires, other tests such as $PaCO_2$, have been investigated. Literature shows that $PaCO_2$ is not an accurate indicator of the presence of OSA. However, elevated $PaCO_2$ is important for perioperative risk stratification and can be used as part of a diagnostic tool for OHS in a patient with OSA (**Table 1**, Q 1.14)[18;76;77]. OHS is a condition in which obese patients fail to maintain adequate levels of ventilation (minute ventilation), leading to oxygen desaturation and high CO_2 levels. OHS is a triad of three components existing of BMI above 30 kg/m^2, daytime hypoxemia and CO_2 elevation. While the prevalence of OHS is reported to be as high as 20% among obese OSA patients, it is often underrecognized. The coexistence of OHS and OSA is associated with a higher morbidity and mortality rate after bariatric surgery. Therefore, OHS should be screened for in bariatric patients with OSA (**Table 1**, Q 1.18)[78-85]. This higher complication rate was also shown in a more recent article[83]. To accomplish the aim of screening for coexistence of OHS, it is recommended to perform venous $HCO3^-$ measurements as part of the routine screening (**Table 1**, Q 1.16)[84;86;87]. A $HCO3^-$ cutoff > 27 mmol/l has a sensitivity and specificity of approximately 86% and 90% respectively, for diagnosing OHS. In addition, it is recommended to include CO_2 measurements in future prospective trials assessing the relation of OHS with perioperative complications and evaluating its role in the risk stratification in bariatric surgery (**Table 1**, Q 1.15).

Taking these matters into consideration, mandatory OSA screening appears indicated due to the high prevalence of OSA in morbidly obese subjects and the increased risk of perioperative complications. While the gold standard to diagnose OSA is a PSG, other tools such as the STOP-Bang questionnaire could be used to identify high risk patients, with portable type 3 sleep studies adding additional information.

Another interesting topic is the coexistence of other comorbidities. The presence of neuromuscular disorders involving the respiratory muscles or advanced obstructive lung diseases should be considered in the preoperative screening. While there is little direct evidence as yet regarding their influence, any combination might increase the perioperative risk of hypoventilation and upper airway obstruction (**Table 1**, Q 1.21)[80;88;89].

Finally, there is no evidence that patients should be specifically investigated for venous thromboembolisms (VTE), unless they have a history of prior deep VTE and/or coagulation disorders (**Table 1**, Q 1.22)[90].

Treatment (Table 2)

The use of CPAP in the perioperative period has shown to be effective in reducing perioperative pulmonary complications and is therefore the most prescribed treatment for OSA (**Table 2**, Q 2.8) [31;36;41;91-97]. Consequently, it is recommended to use CPAP perioperatively in patients with a preoperative AHI ≥ 15/hour, defining moderate to severe OSA (**Table 2**, Q 2.1)[91]. Besides using CPAP to reduce the pulmonary complication risk, CPAP usage is advised as a therapeutic tool in patients with previous atrial fibrillation (**Table 2**, Q 2.7)[92;94;98].

As a certain time period is necessary to get used to CPAP, patients should get acclimatized to its use prior to surgery if possible. This may take up to several weeks (**Table 2**, Q 2.4)[40;92;99-102]. On admission for surgery, patients should bring their own

Table 2 - Recommendations and statements concerning OSA treatment in bariatric surgery

Question	Recommendation	% consensus	Quality of evidence	Strength of recommendation
2.1	Perioperative usage of CPAP is recommended in patients with a preoperative AHI ≥ 15/hour, defining moderate to severe OSA	100	☒☐☐☐	Weak
2.3	Positional therapy is recommended in patients with positional OSA who cannot tolerate CPAP	100	☒☒☒☐	Strong
2.4	It is recommended to let patients get acclimatized to CPAP prior to surgery; this may take up to several weeks	100	☒☒☐☐	Weak
2.5	Patients should bring their own CPAP machine and mask to the hospital; adequate observation of its efficacy is required as requirements may change in the postoperative setting	100	☒☐☐☐	Strong
2.6	Choice of nasal versus full-face CPAP systems should be based on patient comfort and efficacy	100	☒☐☐☐	Strong
2.7	Preoperative CPAP usage is recommended as a risk reduction tool in patients with previous atrial fibrillation	87	☒☐☐☐	Weak
2.8	CPAP is effective in reducing perioperative pulmonary complications and is therefore the most prescribed treatment for OSA	93	☒☒☒☐	Strong
2.9	If patients use MAD prior to surgery, it is recommended that they continue efficacious MAD usage postoperatively	100	☒☐☐☐	Strong

Question 2.2 was excluded

AHI = Apnea Hypopnea Index; CPAP = Continuous Positive Airway Pressure; MAD = Mandibular Advancement Devise; OSA = Obstructive Sleep Apnea

CPAP machine and mask to the hospital. Adequate observation of its efficacy is required, as pressure requirements may change in the postoperative setting (**Table 2**, Q 2.5)[31;33;100;103]. During admission, its efficacy can be assessed by continuously monitoring vital signs and SaO2. After discharge, a more appropriate method is to assess airway efficacy and compliance from downloaded data from the CPAP device.

Choice of nasal versus full-face CPAP systems should be based on patient comfort and efficacy (**Table 2**, Q 2.6). Next to CPAP, other treatment strategies are available. Positional therapy is recommended in patients with positional OSA who cannot tolerate CPAP (**Table 2**, Q 2.3)[24]. Another evidence based non-CPAP device is a mandibular advancement device (MAD)[42]. If patients use MAD prior to surgery, it is recommended that they continue efficacious MAD usage postoperatively (**Table 2**, Q 2.9)[104-106].

Postoperative monitoring (Table 3)

Observation and monitoring are essential during and after surgery to decrease perioperative risks. Requirements depend on the type of surgery and patients' comorbidities. Patients who undergo minor surgery and those without comorbidities are often transferred to the general surgical ward in the postoperative setting. These wards generally only have the capability for intermittent vital parameter measurements. Bariatric surgery patients with OSA are at increased risk of complications and should be continuously monitored in the early postoperative period until they are no longer at risk of respiratory depression (**Table 3**, Q 3.1)[36;38;40;92;99;107-110]. The minimum required monitoring is a pulse oximeter, but there may be a role for additional monitoring such as heart rate, blood pressure, respiratory rate and end-tidal carbon dioxide, especially in patients receiving postoperative narcotics (**Table 3**, Q 3.15)[39;40]. The risk of postoperative complications is even greater in patients who are male, aged above 50 years and have a BMI $\geq$ 60 kg/m^2 (**Table 3**, Q 3.2)[32;41;101;107;109;111;112].

To identify high risk patients and to determine subsequent appropriate management, there is a role for a prolonged stay in the Post Anesthesia Care Unit (PACU) (**Table 3**, Q 3.9). A designated surgical ward with the capability of continuous oxygen saturation measurements, or Medium Care Unit (MCU) should be present in order to accomplish adequate postoperative care. Routine admission of OSA patients to the Intensive Care Unit (ICU) is not necessary (**Table 3**, Q 3.3)[36;38;40;41;108;109;113]. These monitoring recommendations are independent from CPAP usage as CPAP compliance is not guaranteed. The usage of CPAP should go along with monitoring in OSA patients. If CPAP is used, monitoring is still recommended (**Table 3**, Q 3.7)[36;108].

Length of stay in the monitored environment is dependent on several factors, including opioids requirements, and generally varies between the day of surgery and two days postoperatively. An absolute contraindication to outpatient surgery in morbidly obese OSA patients is the absence of a suitable home caregiver (**Table 3**, Q 3.12). Presently, there is no absolute AHI cutoff that would be a contraindication to

Table 3 - Recommendations and statements concerning postoperative monitoring of OSA patients in bariatric surgery

Question	Recommendation	% consensus	Quality of evidence	Strength of recommendation
3.1	Continuous monitoring is recommended in patients with OSA in the early postoperative period until they are no longer at risk of respiratory depression	100	⊠⊠⊠☐	Strong
3.2	Patients who are either male, aged above 50 or have a BMI > 60 kg/m^2 and/or had open surgery are at higher risk of postoperative complications	100	⊠⊠⊠☐	Statement
3.3	Routine admission of OSA patients to the ICU is not necessary	93	⊠⊠⊠☐	Strong
3.7	Monitoring recommendations are independent from CPAP usage as CPAP compliance is not guaranteed; CPAP usage should go along with monitoring	93	⊠⊠⊠☐	Strong
3.9	There is a role for prolonged stay in the PACU to identify high risk patients and to determine subsequent appropriate management	93	⊠☐☐☐	Statement
3.12	Absence of a suitable home caregiver is an absolute contraindication to outpatient surgery in morbidly obese OSA patients	100	⊠☐☐☐	Strong
3.13	There is no absolute AHI cutoff that would be an contraindication to outpatient surgery in OSA patients compliant with CPAP, without severe comorbidities and not requiring opioids or sedatives	79	⊠☐☐☐	Weak
3.14	Postoperative care should not be different for different bariatric procedures	100	⊠☐☐☐	Strong
3.15	The minimum required monitoring is a pulse oximeter, but there may be a role for additional monitoring, especially in patients receiving postoperative narcotics	100	⊠⊠☐☐	Strong

Question 3.4, 3.5, 3.6, 3.8, 3.10 and 3.11 were excluded

AHI = Apnea Hypopnea Index; BMI = Body Mass Index; CPAP = Continuous Positive Airway Pressure; ICU = Intensive Care Unit; OSA = Obstructive Sleep Apnea; PACU = Post Anesthesia Care Unit

outpatient surgery in OSA patients compliant with CPAP, without severe comorbidities and not requiring opioids or sedatives (**Table 3**, Q 3.13).

Finally, postoperative care should not be different for patients based on the choice of operation (**Table 3**, Q 3.14). It is hypothesized, but not documented, that the type of surgery has no influence on OSA related perioperative outcomes, whereas the length of the operation, the approach (open or laparoscopic) and level of expertise of the center may influence outcomes (**Table 1**, Q 1.20).

Anesthetic care (Table 4)

An important aspect of the perioperative management is anesthetic care. As OSA increases risk of perioperative complications, anesthesiologists should assess risk and take precautions to ensure patient safety[3;4].

Optimal anesthetic care starts in the preoperative area where the patient is assessed by the anesthesiology team. Within the operating room, special attention is placed on the optimal positioning of the patient. The ramped position is the preferred position for induction and intubation as morbidly obese patients with diagnosed OSA should be considered at increased risk for difficult intubation. This position improves oxygenation and the laryngoscopic view during intubation. Other positions such as the flat supine position should be avoided in morbidly obese patients who may desaturate readily if there are difficulties with mask ventilation or intubation, because of the effects of obesity on lung volumes and thereby oxygen stores and gas exchange (**Table 4**, Q 4.1)[93;114-117].

Videolaryngoscopy is available for patients in whom there is a concern for a difficult intubation, although routine usage may not be necessary in morbidly obese OSA patients (**Table 4**, Q 4.3). CPAP is strongly recommended at induction in the diagnosed moderately severe and severe OSA patient to maintain lung capacity and reduce time to oxygen desaturation (**Table 4**, Q 4.10)[25;114;115;118;119]. Additionally, high flow oxygenation could be considered in patients with predicted potential for airway difficulties during induction (**Table 4**, Q 4.4).

Further considerations are related to drug use before and during induction. Sedatives as premedication should be avoided in patients with OSA. Opioid analgesia, if used at all, should be titrated slowly and patients should be monitored carefully (**Table 4**, Q 4.2)[115].

At the end of the surgical procedure, patients should only be extubated when close to fully awake, i.e. opening their eyes and coughing well, with neuromuscular blockade fully reversed and muscle function restored (**Table 4**, Q 4.8 + 4.13)[99;104;116;120].

In the postoperative setting, the use of opioids should be minimized and if needed, used with caution (**Table 4**, Q 4.5)[94;99;104;115;116;121-129]. A multimodal analgesic model minimizing the necessity for the administration of opioids includes the use of paracetamol, non-steroidal anti-inflammatory drugs, local anesthetics for incisional infiltration, epidural analgesia and peripheral nerve blocks. Although other strategies such as ketamine, magnesium, intravenous lidocaine and alpha 2-agonists like

Table 4 - Recommendations and statements concerning anesthetic care of OSA patients in bariatric surgery

Question	Recommendation	% consensus	Quality of evidence	Strength of recommendation
4.1	The ramped position is preferred for induction and intubation; avoid flat supine position	100	⊠□□□	Strong
4.2	Avoid sedatives as premedication; opioid analgesia, if used at all, should be titrated slow and patient should be monitored carefully	100	⊠□□□	Strong
4.3	Videolaryngoscopy is available when there are concerns for difficult intubation; routine usage may not be necessary	100	⊠□□□	Weak
4.4	High flow oxygenation could be considered in patients with predicted potential for airway difficulties during induction	100	⊠□□□	Weak
4.5	Postoperative use of opioids should be minimized and if needed used with caution	100	⊠□□□	Strong
4.6	Alternatives for opioids are paracetamol, NSAIDs, local anesthetics for incisional infiltration, epidural analgesia and peripheral nerve blocks	94	⊠□□□	Strong
4.7	Ketamine, magnesium, lidocaine and alpha 2-agonists seem promising, yet high quality supportive evidence regarding their use in this setting is lacking	86	⊠□□□	Weak
4.8	At the end of the surgical procedure, patients should be as fully awake as soon as possible, without sedative effects, opioids and neuromuscular weakness	94	⊠□□□	Strong
4.10	CPAP is strongly recommended at induction in the diagnosed moderately severe OSA patient to maintain lung capacity and reduce time to oxygen desaturation	94	⊠⊠□□	Strong
4.11	ERABS principles should be a standard of practice in the morbidly obese patient	100	⊠□□□	Strong

Table 4 - Recommendations and statements concerning anesthetic care of OSA patients in bariatric surgery (continued)

Question	Recommendation	% consensus	Quality of evidence	Strength of recommendation
4.13	The patient should only be extubated when close to fully awake, i.e. opening their eyes and coughing well, with neuromuscular blockade fully reversed and muscle function restored	94	⊠□□□	Strong
4.16	In the immediate postoperative period, CPAP treatment may be beneficial, particularly in the patient with severe OSA; when needed, CPAP could be supported by increasing oxygen therapy	100	⊠□□□	Strong
4.17	Instead of CPAP, non-invasive ventilation should be considered if there is persistent CO_2 retention postoperatively	100	⊠□□□	Strong
4.19	When practical and as an adjunct for postoperative pain management, regional anesthesia should be considered as part of multimodal analgesia in open weight loss surgery	93	⊠□□□	Weak

Question 4.9, 4.12, 4.14, 4.15, 4.18 and 4.20 were excluded
BiPAP = Bilevel Positive Airway Pressure; CPAP = Continuous Positive Airway Pressure; ERABS = Enhanced Recovery After Bariatric Surgery; NIV = Non Invasive Ventilation; NSAIDs = Non-Steroidal Anti-Inflammatory Drugs

clonidine and dexmedetomidine seem promising, high quality supportive evidence regarding their use in this setting is lacking (**Table 4**, Q 4.6)[94;104;115;116;121;122;124;127]; (**Table 4**, Q 4.7)[115;116;122;123;127;130]. When practical and as an adjunct for postoperative pain management, regional anesthesia should be considered as part of multimodal analgesia in open weight loss surgery (**Table 4**, Q 4.19)[115;116;121;122].

In the immediate postoperative period, CPAP treatment may be beneficial particularly in the patient with severe OSA. When needed, CPAP could be supported by oxygen therapy (**Table 4**, Q 4.16). Instead of CPAP, non-invasive ventilation should be considered if there is persistent CO_2 retention postoperatively (**Table 4**, Q 4.17).

Lastly, enhanced recovery after bariatric surgery (ERABS) principles should be a standard of care in morbidly obese patients (**Table 4**, Q 4.11).

Follow-up (Table 5)

While OSA increases the perioperative risk in bariatric surgery, bariatric surgery decreases the OSA severity in the long-term. The majority of OSA patients (80%) show improvement of their disease with weight loss[131]. The elimination of OSA is defined as a postoperative AHI < 5/hour and is more common in preoperatively diagnosed mild OSA than severe OSA disease (54% versus 18%)[132]. Moreover, in at least three-quarter of patients with a preoperative AHI ≥ 15/hour, the AHI is reduced below 15/hour during follow-up. This implies that around 75% of the preoperatively CPAP dependent patients become CPAP independent after bariatric surgery[133]. Prior to the decision to discontinue CPAP, a patient should be re-evaluated (**Table 5**, Q 5.1)[132;134-136]. Currently, there are no reliable screening tools to assess for residual disease in the postoperative setting (**Table 5**, Q 5.4)[137;138]. Therefore, postoperative in-laboratory PSG or home evaluation is recommended. The timing should be dependent on weight loss and patient symptoms (**Table 5**, Q 5.2)[132;138;139]. A reduction of required CPAP pressure might be helpful in timing postoperative PSG. Patients should continue their OSA therapy until objectively documented to be free of OSA (**Table 5**, Q 5.7)[135;138-141]. In case of persistent OSA, the patient should be managed according to conventional therapy (**Table 5**, Q 5.8)[132;135;138].

Compliance is known to be a challenge in these patients. It has been reported that up to 50-60% of moderately-severe to severe OSA patients do not attend postoperative PSG or portable monitoring[24;133]. In addition to the low compliance in follow-up, previous reports have shown that up to 70% of patients are non-compliant with their CPAP therapy in the long-term[142].

To increase adherence, counselling on the importance of compliance, follow-up testing and information regarding alternative OSA therapies to CPAP should begin prior to surgery (**Table 5**, Q 5.5). Adequate education of care givers and preoperative counseling for patients should address this matter and align patient expectations with realistic outcomes (**Table 5**, Q 5.6)[135].

Surgically induced weight loss not only decreases OSA severity but also OHS severity. OHS related decreased expiratory reserve volume normalizes following surgical induced weight loss. Multiple studies have showed that this weight loss improved arterial blood gases, hemodynamic function and lung volumes in OHS patients[143-146].

Table 5 - Recommendations and statements concerning follow-up of OSA in bariatric surgery

Question	Recommendation	% consensus	Quality of evidence	Strength of recommendation
5.1	Prior to the decision to discontinue CPAP, a patient should be re-evaluated	93	⊠⊠□□	Strong
5.2	PSG the recommended test to assess for residual disease in the postoperative setting; timing should be dependent on weight loss and patient symptoms	66*	⊠□□□	Weak
5.4	Currently, there are no other reliable screening tools to assess for residual disease in the postoperative setting	93	⊠□□□	Statement
5.5	Counseling on the importance of compliance, follow-up testing and information regarding alternative OSA therapies to CPAP should begin prior to bariatric surgery	66*	⊠□□□	Strong
5.6	Adequate education of care givers and preoperative counseling for patients should address this matter and align patient expectations with realistic outcomes	100	⊠□□□	Strong
5.7	Patients should continue their OSA therapy until objectively documented to be free of OSA	87	⊠□□□	Weak
5.8	In case of persistent OSA, the patient should be managed according to conventional therapy	93	⊠□□□	Strong

* Consensus level < 70%

Question 5.3 was excluded

CPAP = Continuous Positive Airway Pressure; OSA = Obstructive Sleep Apnea

DISCUSSION

While independent guidelines were available for both bariatric surgery and OSA management[2;103], this was the first international consensus meeting regarding the perioperative management of OSA in bariatric surgery. The 58 formulated recommendations and statements resulting from this meeting serve as a guideline for all physicians involved in the treatment of morbidly obese patients with OSA scheduled for (bariatric) surgery requiring general anesthesia. Consensus was reached for 55 statements and recommendations, whereas three recommendations reached no consensus. 'CPAP is advisable to reduce the incidence of perioperative complications and CV risks' reached 64% consensus. Two other recommendations in the follow-up topic reached 66% consensus. All three recommendations had a 'very low' quality of evidence which was likely to be the cause of no consensus. This should encourage researchers to perform more research on these topics.

As OSA is one of the most prevalent comorbidities among morbidly obese subjects and the number of procedures in morbidly obese patients is increasing worldwide, the meeting was timely and its results are likely to be valuable in the surgical management of these patients. By providing recommendations that are directly applicable in the clinical setting, the recommendations in this manuscript could lead to more standardized care of these patients.

The "Amsterdam Delphi Method" has several limitations. Due to the need of the numerous questions being addressed, a strict time schedule was required and prolonged discussions were not possible. It is possible that some questions might not have been fully addressed. In the expert face-to-face setting, anonymity is not feasible. While this setting leads to extensive discussion and sharing of experts' opinion, an experts' vote could possibly be influenced by the voting of the other experts. This may have caused bias to the results. Only articles written in English were considered eligible for inclusion. Since bariatric surgery is increasingly being performed in the Middle-East and Latin America, relevant papers written in other languages might have been missed due to this language restriction.

Since the last literature search was performed in December 2015, articles published after this date were not systematically included. Also, literature with a high level of evidence was often not available to answer certain questions, resulting in recommendations based on expert opinion. Nevertheless, due to a multidisciplinary approach including experts with extensive experience in the field of OSA in morbidly obese patients, recommendations from the experts are the best level of evidence available. Furthermore, the areas of clinical care where there is a paucity of evidence, should challenge physicians and researchers to perform more research on these topics.

Future exploration in this field should address the major gaps that were identified during the present meeting. As routine preoperative PSG measurements are not universally feasible, one of the major challenges is to develop a reliable alternative

diagnostic method that can be more readily adopted. Although the AHI is a commonly used metric of severity, the value of other metrics such as the length of apneas, degree of oxygen desaturation and percentage of apneas versus hypopneas need further evaluation as these parameters might have a role in the prediction of OSA severity, including the propensity to arouse in response to events, and thus perioperative risk.

Additionally, physicians should be mindful of the possible coexistence of OHS in patients with OSA presenting for bariatric surgery. The inclusion of CO_2 measurements should be addressed in future prospective trials. Another major challenge for the anesthesiologists is to minimize opioids in the perioperative care. While some new alternatives such as ketamine, lidocaine, magnesium and alpha 2-agonists seem promising, the benefits of these agents should be evaluated in larger cohorts or prospective studies.

Study questions that were raised after the meeting are not mentioned in the results section. One of these include time of re-initiation of CPAP ventilation after surgery. Some surgeons raise the doubt that the positive pressure insufflated into the upper airways can cause an increase in intra-gastric pressure with an increased risk of anastomotic or staple line leakage. Ramirez and colleagues evaluated the influence of postoperative CPAP usage on anastomotic or staple line leakage in 310 bariatric patients (91 (29.3%) with CPAP). While the authors concluded that CPAP was not associated with increased morbidity, they stated that their sample size was too small and a larger series would be necessary to assess the differences between groups[147]. This was in similarity with few older studies with smaller sample sizes[108;148].

Another interesting topic is the influence of OSA on type II diabetes. Evidence for an association for OSA and glucose metabolic dysfunction is rapidly growing[149]. CPAP treatment improves glucose metabolism, lowers blood pressures and has benefits in controlling insulin sensitivity[150-153]. The value of diagnosing type II diabetes preoperatively and the effect of OSA on type II diabetes remission after surgery should be evaluated in future studies.

In conclusion, this consensus meeting resulted in 58 recommendations and statements concerning the perioperative care of OSA patients undergoing bariatric surgery, providing guidance to physicians that will help optimize the perioperative care and safety.

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Supplementary material I - Literature searches

Topic 1.
Bariatric surgery:
(Bariatrics [Mesh] OR bariatric*[tiab] OR gastric bypass*[tiab] OR Roux-en-Y[tiab] OR LRYGB*[tiab] OR RYGB*[tiab] OR gastrojejunostom*[tiab] OR bilio pancreati*[tiab] OR duodenal switch*[tiab] OR BPD-DS[tiab] OR gastric sleeve*[tiab] OR sleeve gastrectom*[tiab] OR gastric band*[tiab] OR LABG*[tiab] OR biliopancreati*[tiab]) AND ("Sleep Apnea, Obstructive"[Mesh] OR OSA[tiab] OR OSAS[tiab] OR apnoea*[tiab] OR apnea*[tiab] OR hypopnea*[tiab] OR hypopnoea*[tiab] OR apneic*[tiab] OR apnoeic*[tiab] OR SDB[tiab] OR sleep-disordered[tiab] OR "Snoring"[Mesh] OR snoring*[tiab] OR snore*[tiab]) AND ("Prevalence"[Mesh] OR "Epidemiology"[Mesh] OR "Incidence"[Mesh] OR prevalen*[tiab] OR epidem*[tiab] OR inciden*[tiab] OR "Intraoperative Complications"[Mesh] OR "Postoperative Complications"[Mesh] OR complicat*[tiab] OR adverse effect*[tiab] OR risk*[tiab] OR ((polysomnograph*[tiab] OR "Polysomnography"[Mesh] OR PSG[tiab] OR somnograph*[tiab]) AND ("Diagnosis"[Mesh] OR diagnos*[tiab] OR exam*[tiab] OR assess*[tiab] OR determin*[tiab])) OR polygraph* OR PG OR "Questionnaires"[Mesh] OR questionnair*[tiab] OR survey*[tiab] OR stop-bang[tiab] OR ESS[tiab] OR epworth sleepiness scale*[tiab] OR ((diagnos*[tiab] OR screen*[tiab] OR examin*[tiab] OR asses*[tiab] OR determin*[tiab]) AND (clinical symp*[tiab] OR sleepiness[tiab])) OR "Carbon Dioxide"[Mesh] OR carbon diox*[tiab] OR PaCO2[tiab] OR CO2[tiab] OR PCO2[tiab] OR "Bicarbonates"[Mesh] OR bicarbon*[tiab] OR hydrogen carbonat*[tiab] OR carbonic acid ion*[tiab] OR HCO3[tiab] OR (("Anoxia"[Mesh] OR anoxia*[tiab] OR hypoxia*[tiab] OR hypoxem*[tiab] OR oxygen deficien*[tiab] OR desaturat*[tiab] OR ODI[tiab] OR obstructive event*[tiab] OR hypoventilat*[tiab] OR respiratory distress index*[tiab] OR RDI[tiab]) AND (sever*[tiab])) OR ((Apnea hypopnea index*[tiab] OR AHI[tiab]) AND (index*[tiab] OR level*[tiab] OR cut off*[tiab] OR rate[tiab] OR rates[tiab])))

Morbid obesity:
("Obesity, Morbid"[Mesh] OR ((severe[tiab] OR morbid*[tiab]) AND (obes*[tiab]))) AND ("Sleep Apnea, Obstructive"[Mesh] OR OSA[tiab] OR OSAS[tiab] OR apnoea*[tiab] OR apnea*[tiab] OR hypopnea*[tiab] OR hypopnoea*[tiab] OR apneic*[tiab] OR apnoeic*[tiab] OR SDB[tiab] OR sleep-disordered[tiab] OR "Snoring"[Mesh] OR snoring*[tiab] OR snore*[tiab]) AND ("Prevalence"[Mesh] OR "Epidemiology"[Mesh] OR "Incidence"[Mesh] OR prevalen*[tiab] OR epidem*[tiab] OR inciden*[tiab] OR "Intraoperative Complications"[Mesh] OR "Postoperative Complications"[Mesh] OR complicat*[tiab] OR adverse effect*[tiab] OR risk*[tiab] OR ((polysomnograph*[tiab] OR "Polysomnography"[Mesh] OR PSG[tiab] OR somnograph*[tiab]) AND ("Diagnosis"[Mesh] OR diagnos*[tiab] OR exam*[tiab] OR assess*[tiab] OR determin*[tiab])) OR polygraph* OR PG OR "Questionnaires"[Mesh] OR questionnair*[tiab] OR survey*[tiab] OR stop-bang[tiab] OR ESS[tiab] OR epworth sleepiness scale*[tiab] OR ((diagnos*[tiab] OR screen*[tiab] OR examin*[tiab] OR asses*[tiab] OR determin*[tiab]) AND (clinical symp*[tiab] OR sleepiness[tiab])) OR "Carbon Dioxide"[Mesh] OR carbon diox*[tiab] OR PaCO2[tiab] OR CO2[tiab] OR PCO2[tiab] OR "Bicarbonates"[Mesh] OR bicarbon*[tiab] OR hydrogen carbonat*[tiab] OR carbonic acid ion*[tiab] OR HCO3[tiab] OR (("Anoxia"[Mesh] OR anoxia*[tiab] OR hypoxia*[tiab] OR hypoxem*[tiab] OR oxygen deficien*[tiab] OR desaturat*[tiab] OR ODI[tiab] OR obstructive event*[tiab] OR hypoventilat*[tiab] OR respiratory distress index*[tiab] OR RDI[tiab]) AND (sever*[tiab])) OR ((Apnea hypopnea index*[tiab] OR AHI[tiab]) AND (index*[tiab] OR level*[tiab] OR cut off*[tiab] OR rate[tiab] OR rates[tiab])))

Topic 2.

Bariatric surgery:

(Bariatrics [Mesh] OR bariatric*[tiab] OR gastric bypass*[tiab] OR Roux-en-Y[tiab] OR LRYGB*[tiab] OR RYGB*[tiab] OR gastrojejunostom*[tiab] OR bilio pancreati*[tiab] OR duodenal switch*[tiab] OR BPD-DS[tiab] OR gastric sleeve*[tiab] OR sleeve gastrectom*[tiab] OR gastric band*[tiab] OR LABG*[tiab] OR biliopancreati*[tiab]) AND ("Sleep Apnea, Obstructive"[Mesh] OR OSA[tiab] OR OSAS[tiab] OR apnoea*[tiab] OR apnea*[tiab] OR hypopnea*[tiab] OR hypopnoea*[tiab] OR apneic*[tiab] OR apnoeic*[tiab] OR SDB[tiab] OR sleep-disordered[tiab] OR "Snoring"[Mesh] OR snoring*[tiab] OR snore*[tiab]) AND ("Continuous Positive Airway Pressure"[Mesh] OR CPAP*[tiab] OR Continuous Positive Airway Pressur*[tiab] OR apnea hypopnea index[tiab] OR AHI[tiab] OR "Supine Position"[Mesh] OR supine[tiab] OR dorsal position*[tiab] OR mandibular*[tiab] OR MAD[tiab] OR oral applianc*[tiab])

Morbid obesity:

("Obesity, Morbid"[Mesh] OR ((severe[tiab] OR morbid*[tiab]) AND (obes*[tiab]))) AND ("Sleep Apnea, Obstructive"[Mesh] OR OSA[tiab] OR OSAS[tiab] OR apnoea*[tiab] OR apnea*[tiab] OR hypopnea*[tiab] OR hypopnoea*[tiab] OR apneic*[tiab] OR apnoeic*[tiab] OR SDB[tiab] OR sleep-disordered[tiab] OR "Snoring"[Mesh] OR snoring*[tiab] OR snore*[tiab]) AND ("Continuous Positive Airway Pressure"[Mesh] OR CPAP*[tiab] OR Continuous Positive Airway Pressur*[tiab] OR apnea hypopnea index[tiab] OR AHI[tiab] OR "Supine Position"[Mesh] OR supine[tiab] OR dorsal position*[tiab] OR mandibular*[tiab] OR MAD[tiab] OR oral applianc*[tiab])

Topic 3.
Bariatric surgery:
(Bariatrics [Mesh] OR bariatric*[tiab] OR gastric bypass*[tiab] OR Roux-en-Y[tiab] OR LRYGB*[tiab] OR RYGB*[tiab] OR gastrojejunostom*[tiab] OR bilio pancreati*[tiab] OR duodenal switch*[tiab] OR BPD-DS[tiab] OR gastric sleeve*[tiab] OR sleeve gastrectom*[tiab] OR gastric band*[tiab] OR LABG*[tiab] OR biliopancreati*[tiab]) AND ("Sleep Apnea, Obstructive"[Mesh] OR OSA[tiab] OR OSAS[tiab] OR apnoea*[tiab] OR apnea*[tiab] OR hypopnea*[tiab] OR hypopnoea*[tiab] OR apneic*[tiab] OR apnoeic*[tiab] OR SDB[tiab] OR sleep-disordered[tiab] OR "Snoring"[Mesh] OR snoring*[tiab] OR snore*[tiab]) AND ("Postoperative Period"[Mesh] OR "Postoperative Care"[Mesh] OR postoperat*[tiab] OR post operat*[tiab] OR after surg*[tiab] OR post surg*[tiab] OR postsurg*[tiab] OR "Monitoring, Physiologic"[Mesh] OR monitor*[tiab] OR "Intensive Care Units"[Mesh] OR Intensive Care*[tiab] OR ICU[tiab] OR medium care*[tiab] OR MCU[tiab] OR (("Continuous Positive Airway Pressure"[Mesh] OR CPAP*[tiab] OR Continuous Positive Airway Pressur*[tiab]) AND ("Patient Compliance"[Mesh] OR complian*[tiab] OR adherenc*[tiab])) OR post anesthesia care uit*[tiab] OR PACU[tiab] OR "Recovery Room"[Mesh] OR Recovery[tiab] OR "Ambulatory Surgical Procedures"[Mesh] OR ambulator*[tiab] OR outpatient*[tiab] OR Same day*[tiab] OR Day surg*[tiab] OR Day time*[tiab])

Morbid obesity:
("Obesity, Morbid"[Mesh] OR ((severe[tiab] OR morbid*[tiab]) AND (obes*[tiab]))) AND ("Sleep Apnea, Obstructive"[Mesh] OR OSA[tiab] OR OSAS[tiab] OR apnoea*[tiab] OR apnea*[tiab] OR hypopnea*[tiab] OR hypopnoea*[tiab] OR apneic*[tiab] OR apnoeic*[tiab] OR SDB[tiab] OR sleep-disordered[tiab] OR "Snoring"[Mesh] OR snoring*[tiab] OR snore*[tiab]) AND ("Postoperative Period"[Mesh] OR "Postoperative Care"[Mesh] OR postoperat*[tiab] OR post operat*[tiab] OR after surg*[tiab] OR post surg*[tiab] OR postsurg*[tiab] OR "Monitoring, Physiologic"[Mesh] OR monitor*[tiab] OR "Intensive Care Units"[Mesh] OR Intensive Care*[tiab] OR ICU[tiab] OR medium care*[tiab] OR MCU[tiab] OR (("Continuous Positive Airway Pressure"[Mesh] OR CPAP*[tiab] OR Continuous Positive Airway Pressur*[tiab]) AND ("Patient Compliance"[Mesh] OR complian*[tiab] OR adherenc*[tiab])) OR post anesthesia care uit*[tiab] OR PACU[tiab] OR "Recovery Room"[Mesh] OR Recovery[tiab] OR "Ambulatory Surgical Procedures"[Mesh] OR ambulator*[tiab] OR outpatient*[tiab] OR Same day*[tiab] OR Day surg*[tiab] OR Day time*[tiab])

Topic 4.

Bariatric surgery:

(Bariatrics [Mesh] OR bariatric*[tiab] OR gastric bypass*[tiab] OR Roux-en-Y[tiab] OR LRYGB*[tiab] OR RYGB*[tiab] OR gastrojejunostom*[tiab] OR bilio pancreati*[tiab] OR duodenal switch*[tiab] OR BPD-DS[tiab] OR gastric sleeve*[tiab] OR sleeve gastrectom*[tiab] OR gastric band*[tiab] OR LABG*[tiab] OR biliopancreati*[tiab]) AND ("Sleep Apnea, Obstructive"[Mesh] OR OSA[tiab] OR OSAS[tiab] OR apnoea*[tiab] OR apnea*[tiab] OR hypopnea*[tiab] OR hypopnoea*[tiab] OR apneic*[tiab] OR apnoeic*[tiab] OR SDB[tiab] OR sleep-disordered[tiab] OR "Snoring"[Mesh] OR snoring*[tiab] OR snore*[tiab]) AND ("Anesthesia"[Mesh] OR anesthes*[tiab] OR "Intubation"[Mesh] OR intubat*[tiab] OR "Airway Extubation"[Mesh] OR extubation*[tiab] OR induction*[tiab] OR "Patient Positioning"[Mesh] OR position*[tiab] OR "Preanesthetic Medication"[Mesh] OR preanesthetic*[tiab] OR premedicati*[tiab] OR "Laryngoscopy"[Mesh] OR laryngoscop*[tiab] OR "Analgesics, Opioid"[Mesh] OR opioid*[tiab] OR morphin*[tiab] OR Meperidin*[tiab] OR Hydromorphon*[tiab] OR Alfentanyl*[tiab] OR Fentanyl*[tiab] OR Remifentanil*[tiab] OR Sufenta*[tiab] OR Etorphin*[tiab] OR "Ketamine"[Mesh] OR "Lidocaine"[Mesh] OR "Dexmedetomidine"[Mesh] OR "Clonidine"[Mesh] OR "Nicotine"[Mesh] OR ketamin*[tiab] OR lidocain*[tiab] OR dexmedetomidin*[tiab] OR Nortryptilin*[tiab] OR pregabalin*[tiab] OR Clonidin*[tiab] OR Nabilone*[tiab] OR Nicotin*[tiab] OR non-opioid*[tiab] OR fraction of inspired oxyg*[tiab] OR fio2[tiab] OR non-invasive positive pressure*[tiab] OR Noninvasive positive pressure*[tiab] OR Noninvasive ventilati*[tiab] OR non-invasive ventilati*[tiab] OR NIPP*[tiab] OR Bilevel positive airway*[tiab] OR BIPAP[tiab] OR BI-PAP[tiab] OR "Autonomic Nerve Block"[Mesh] OR "Analgesia, Epidural"[Mesh] OR "Anesthesia, Spinal"[Mesh] OR spinal anesthe*[tiab] OR epidural anesthe*[tiab] OR neuraxial block*[tiab] OR nerve block*[tiab] OR "Neuromuscular Monitoring"[Mesh] OR neuromuscular monitor*[tiab] OR Train of Four*[tiab] OR TOF*[tiab])

Morbid obesity:

("Obesity, Morbid"[Mesh] OR ((severe[tiab] OR morbid*[tiab]) AND (obes*[tiab]))) AND ("Sleep Apnea, Obstructive"[Mesh] OR OSA[tiab] OR OSAS[tiab] OR apnoea*[tiab] OR apnea*[tiab] OR hypopnea*[tiab] OR hypopnoea*[tiab] OR apneic*[tiab] OR apnoeic*[tiab] OR SDB[tiab] OR sleep-disordered[tiab] OR "Snoring"[Mesh] OR snoring*[tiab] OR snore*[tiab]) AND ("Anesthesia"[Mesh] OR anesthes*[tiab] OR "Intubation"[Mesh] OR intubat*[tiab] OR "Airway Extubation"[Mesh] OR extubation*[tiab] OR induction*[tiab] OR "Patient Positioning"[Mesh] OR position*[tiab] OR "Preanesthetic Medication"[Mesh] OR preanesthetic*[tiab] OR premedicati*[tiab] OR "Laryngoscopy"[Mesh] OR laryngoscop*[tiab] OR "Analgesics, Opioid"[Mesh] OR opioid*[tiab] OR morphin*[tiab] OR Meperidin*[tiab] OR Hydromorphon*[tiab] OR Alfentanyl*[tiab] OR Fentanyl*[tiab] OR Remifentanil*[tiab] OR Sufenta*[tiab] OR Etorphin*[tiab] OR "Ketamine"[Mesh] OR "Lidocaine"[Mesh] OR "Dexmedetomidine"[Mesh] OR "Clonidine"[Mesh] OR "Nicotine"[Mesh] OR ketamin*[tiab] OR lidocain*[tiab] OR dexmedetomidin*[tiab] OR Nortryptilin*[tiab] OR pregabalin*[tiab] OR Clonidin*[tiab] OR Nabilone*[tiab] OR Nicotin*[tiab] OR non-opioid*[tiab] OR fraction of inspired oxyg*[tiab] OR fio2[tiab] OR non-invasive positive pressure*[tiab] OR Noninvasive positive pressure*[tiab] OR Noninvasive ventilati*[tiab] OR non-invasive ventilati*[tiab] OR NIPP*[tiab] OR Bilevel positive airway*[tiab] OR BIPAP[tiab] OR BI-PAP[tiab] OR "Autonomic Nerve Block"[Mesh] OR "Analgesia, Epidural"[Mesh] OR "Anesthesia, Spinal"[Mesh] OR spinal anesthe*[tiab] OR epidural anesthe*[tiab] OR neuraxial block*[tiab] OR nerve block*[tiab] OR "Neuromuscular Monitoring"[Mesh] OR neuromuscular monitor*[tiab] OR Train of Four*[tiab] OR TOF*[tiab])

Topic 5.
Bariatric surgery:
(Bariatrics [Mesh] OR bariatric*[tiab] OR gastric bypass*[tiab] OR Roux-en-Y[tiab] OR LRYGB*[tiab] OR RYGB*[tiab] OR gastrojejunostom*[tiab] OR bilio pancreati*[tiab] OR duodenal switch*[tiab] OR BPD-DS[tiab] OR gastric sleeve*[tiab] OR sleeve gastrectom*[tiab] OR gastric band*[tiab] OR LABG*[tiab] OR biliopancreati*[tiab]) AND ("Sleep Apnea, Obstructive"[Mesh] OR OSA[tiab] OR OSAS[tiab] OR apnoea*[tiab] OR apnea*[tiab] OR hypopnea*[tiab] OR hypopnoea*[tiab] OR apneic*[tiab] OR apnoeic*[tiab] OR SDB[tiab] OR sleep-disordered[tiab] OR "Snoring"[Mesh] OR snoring*[tiab] OR snore*[tiab]) AND ("Postoperative Care"[Mesh] OR postoperat*[tiab] OR post operat*[tiab] OR postsurg*[tiab] OR post surg*[tiab] OR after surg*[tiab] OR "Follow-Up Studies"[Mesh] OR followup*[tiab] OR follow up*[tiab] OR longterm*[tiab] OR long term*[tiab]) AND ("Polysomnography"[Mesh] OR polysomnograph*[tiab] OR PSG[tiab] OR somnograph*[tiab] OR "Questionnaires"[Mesh] OR questionnair*[tiab] OR survey*[tiab] OR ((screen*[tiab]) AND (tool*[tiab] OR instrument*[tiab])) OR stop-bang[tiab] OR ESS[tiab] OR epworth sleepiness scale*[tiab] OR (("Continuous Positive Airway Pressure"[Mesh] OR CPAP*[tiab] OR Continuous Positive Airway Pressur*[tiab]) AND ("Patient Compliance"[Mesh] OR complian*[tiab] OR adherenc*[tiab])) OR drug induced sleep endoscop*[tiab] OR DISE[tiab] OR improv*[tiab] OR residual*[tiab] OR reduc*[tiab] cure*[tiab] OR curat*[tiab] OR resolv*[tiab] OR recurr*[tiab] OR increas*[tiab] OR decreas*[tiab] OR enhanc*[tiab] OR progress*[tiab] OR weight loss*[tiab] OR "Weight Loss"[Mesh] OR weight reduct*[tiab] OR BMI loss*[tiab] OR BMI reduct*[tiab])

Morbid obesity:
("Obesity, Morbid"[Mesh] OR ((severe[tiab] OR morbid*[tiab]) AND (obes*[tiab]))) AND ("Sleep Apnea, Obstructive"[Mesh] OR OSA[tiab] OR OSAS[tiab] OR apnoea*[tiab] OR apnea*[tiab] OR hypopnea*[tiab] OR hypopnoea*[tiab] OR apneic*[tiab] OR apnoeic*[tiab] OR SDB[tiab] OR sleep-disordered[tiab] OR "Snoring"[Mesh] OR snoring*[tiab] OR snore*[tiab]) AND ("Postoperative Care"[Mesh] OR postoperat*[tiab] OR post operat*[tiab] OR postsurg*[tiab] OR post surg*[tiab] OR after surg*[tiab] OR "Follow-Up Studies"[Mesh] OR followup*[tiab] OR follow up*[tiab] OR longterm*[tiab] OR long term*[tiab]) AND ("Polysomnography"[Mesh] OR polysomnograph*[tiab] OR PSG[tiab] OR somnograph*[tiab] OR "Questionnaires"[Mesh] OR questionnair*[tiab] OR survey*[tiab] OR ((screen*[tiab]) AND (tool*[tiab] OR instrument*[tiab])) OR stop-bang[tiab] OR ESS[tiab] OR epworth sleepiness scale*[tiab] OR (("Continuous Positive Airway Pressure"[Mesh] OR CPAP*[tiab] OR Continuous Positive Airway Pressur*[tiab]) AND ("Patient Compliance"[Mesh] OR complian*[tiab] OR adherenc*[tiab])) OR drug induced sleep endoscop*[tiab] OR DISE[tiab] OR improv*[tiab] OR residual*[tiab] OR reduc*[tiab] cure*[tiab] OR curat*[tiab] OR resolv*[tiab] OR recurr*[tiab] OR increas*[tiab] OR decreas*[tiab] OR enhanc*[tiab] OR progress*[tiab] OR weight loss*[tiab] OR "Weight Loss"[Mesh] OR weight reduct*[tiab] OR BMI loss*[tiab] OR BMI reduct*[tiab])

Supplementary material II – Voting rounds and definitive percentage of consensus based on number of votes and number of voting experts

Question	Voting round 1	Voting round 2	% consensus
1.1	-	-	-
1.2	9	13	93
1.3	14	-	100
1.4	10	9	64*
1.5	12	12	86
1.6	10	14	100
1.7	7	13	93
1.8	12	14	100
1.9	4	13	93
1.10	1	Excluded	-
1.11	4	Excluded	-
1.12	5	14	100
1.13	-	Excluded	-
1.14	7	14	100
1.15	11	14	100
1.16	13	15	100
1.17	0	12	80
1.18	14	-	100
1.19	2	12	80
1.20	2	14	93
1.21	-	15	100
1.22	5	15	100
1.23	0	14	93
Question	Voting round 1	Voting round 2	% consensus
2.1	10	15	100
2.2	10	Excluded	-
2.3	2	15	100
2.4	2	15	100
2.5	11	15	100
2.6	1	15	100
2.7	10	13	87
2.8	13	14	93
2.9	2	15	100

Supplementary material II – Voting rounds and definitive percentage of consensus based on number of votes and number of voting experts (continued)

Question	Voting round 1	Voting round 2	% consensus
3.1	8	14	100
3.2	7	14	100
3.3	10	13	93
3.4	8	Excluded	-
3.5	Excluded	-	-
3.6	Excluded	-	-
3.7	10	13	93
3.8	Excluded	-	-
3.9	0	13	93
3.10	Excluded	-	-
3.11	4	Excluded	-
3.12	9	14	100
3.13	4	11	79
3.14	14	-	100
3.15	7	14	100
Question	Voting round 1	Voting round 2	% consensus
4.1	13	15	100
4.2	5	15	100
4.3	15	15	100
4.4	5	15	100
4.5	6	15	100
4.6	10	14	94
4.7	5	13	86
4.8	13	14	94
4.9	Excluded	-	-
4.10	8	14	94
4.11	13	15	100
4.12	3	Excluded	-
4.13	0	14	94
4.14	0	Excluded	-
4.15	Excluded	-	-
4.16	9	15	100
4.17	5	15	100
4.18	Excluded	-	-
4.19	4	14	93
4.20	8	Excluded	-

Supplementary material II – Voting rounds and definitive percentage of consensus based on number of votes and number of voting experts (continued)

Question	Voting round 1	Voting round 2	% consensus
5.1	5	14	93
5.2	14	10	66*
5.3	6	Excluded	-
5.4	3	14	93
5.5	9	10	66*
5.6	15	-	100
5.7	11	13	87
5.8	4	14	93

Obstructive sleep apnea and bariatric surgical guidelines: summary and update

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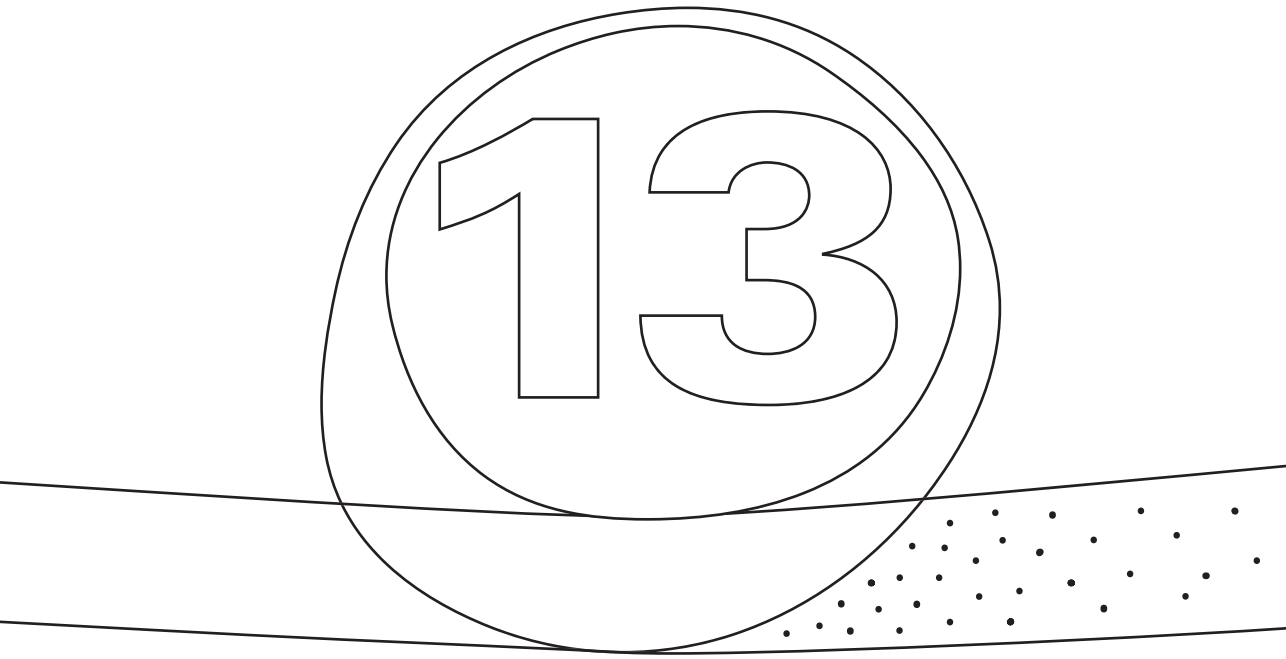

ABSTRACT

Purpose of Review: Increasing numbers of bariatric surgical procedures and the high prevalence of obstructive sleep apnea (OSA) in this population have resulted in a growing interest in the perioperative management of OSA in bariatric surgery. This review provides a summary of the first consensus guideline on this topic as well as an update of the newest literature available.

Recent findings: All bariatric patients should be screened for OSA and obesity hypoventilation syndrome to reduce the risk of perioperative complications. Intraoperative precautions are preoxygenation, induction and intubation in ramped position, continuous positive airway pressure (CPAP) and positive end-expiratory pressure during induction, maintenance of low tidal volumes during surgery, multimodal anesthesia and analgesia with avoidance of opioids and extubation when patients are free of neuromuscular blockage. CPAP therapy and continuous monitoring with a minimum of pulse oximetry is recommended in the early postoperative period.

Summary: Multiple precautions exist to minimize the risk of cardiopulmonary complications and to enhance recovery after surgery. A combination of these procedures seems to provide optimal perioperative care of OSA patients undergoing bariatric surgery. Nearly 75% of recommendations are based on low quality of evidence, indicating the high value of experts' opinion and potential for future research.

INTRODUCTION

Bariatric surgery is a globally used treatment modality for morbid obesity and associated comorbidities. The increasing prevalence of morbid obesity, introduction of standardized techniques and high surgical success rates contribute to the rising number of bariatric surgical procedures. Over 500,000 procedures were performed worldwide in 2013[1].

Studies performing mandatory sleep studies in all patients scheduled for surgery found a 60% incidence of obstructive sleep apnea (OSA)[2]. Nearly 90% of these patients were not aware of their OSA status prior to testing[3]. Patients associating symptoms of loud snoring and severe daytime sleepiness with their obesity rather than OSA could be an important factor for this under diagnosis.

Recognizing OSA is an important aspect of the perioperative care of bariatric patients. Both morbid obesity and OSA are risk factors for intraoperative difficulties; i.e. intubation and postoperative complications. Desaturations, cardiac arrest, respiratory failure and unexpected Intensive Care Unit (ICU) admissions occur more often in OSA than non-OSA patients. Increasing numbers of bariatric surgical procedures and the high prevalence of OSA in this population have resulted in a growing interest in the perioperative management of OSA in bariatric surgery.

The first international consensus meeting on this topic was held in Amsterdam, the Netherlands, in March 2016. Over 7300 articles were systematically screened on title and abstract. This resulted in a final inclusion of ten to 119 articles in each of the five main topics, including preoperative screening, treatment, postoperative monitoring, anesthetic care and follow-up. Nearly 75% of recommendations and statements had a poor or low quality of evidence, illustrating the importance of experts' opinion and potential to perform more high quality research. By collecting experts' opinion based on their knowledge and experience, two-third of recommendations with a poor or low quality of evidence could still be graded as strong[2].

The aim of this review is to present a summary of the most important aspects in perioperative care and to provide an update on the newest relevant literature available.

The bariatric surgical patient; what we need to know

Over 10% of the world's population is struggling with obesity in daily life[4]. Authorities are stimulated to offer programs for obesity prevention and weight loss. Bariatric surgery has been introduced to tackle overweight and related negative life expectancy. When performing bariatric surgery, one must not forget that morbid obesity is a risk factor for comorbid conditions in the operating rooms. These difficulties can be divided in mechanical problems i.e. OSA and difficult airway and metabolic problems such as hypertension, dyslipidemia and type II diabetes. A combination of these factors, often occurring in bariatric patients, illustrate the clinical challenge in the perioperative setting[5]. Anesthesiologists should be aware of the anatomical, physiological, metabolic and pharmacological changes caused by obesity. A very important physiologic

characteristic is the time to desaturation. Benumof and colleagues illustrated the rapid desaturation in obese subjects following 1mg/kg intravenous succinylcholine. The time to SaO2 = 80% was reached after 3.1 minutes and was even shorter than the time to desaturation in a 10-kg child (3.7 minutes) or a moderately ill 70-kg adult (5.5 minutes)[6]. This could be explained by the high oxygen consumption and low alveolar volume in relation to weight. Other negatively affected respiratory components including compliance, neuromuscular strength and work of breathing cause obese patients to be at risk of the development of pulmonary complications after bariatric surgery[7].

OSA is the most common sleep breathing disorder in morbidly obese and has an additional negative effect on cardiopulmonary functions. Fourteen prospective studies primarily investigated the prevalence of OSA in the bariatric population. Of these studies, eleven found a prevalence over 60%[2]. An overnight laboratory polysomnography is considered the gold standard for OSA diagnosis. Type 3 polygraphy is a reliable alternative in the bariatric population with a high pre-test probability. These sleep studies generate two accurate measurements for OSA diagnosis; the apnea-hypopnea-index (AHI) and oxygen desaturation index (ODI). Bariatric clinics not performing mandatory sleep studies are recommended to use the STOP-Bang or Berlin questionnaire to stratify the risk for OSA. Important notes are that none of existing questionnaires reaches a 100% sensitivity and a sleep study is required to diagnose definite OSA and its severity.

Obesity hypoventilation syndrome (OHS) is a second sleep breathing disorder which is characterized by alveolar hypoventilation due to respiratory mechanics, a blunted central drive to response to hypercapnia, hypoxemia and leptin resistance. The pathophysiology of this diminished central drive is unclear, but sleep disorders such as OSA play an important role. OSA treatment partly corrects the negative effects of OHS suggesting that upper airway obstruction and flow limitation are important factors in the pathogenesis of OHS[7]. OHS is an independent risk factor for more severe desaturations and is present in 20% of OSA patients. The combination of OSA and OHS is associated with higher morbidity and mortality[8;9]. In agreement with the consensus report published in 2016[2], more recent papers recommend OHS screening through venous $HCO3^-$ in all bariatric patients considering the high mortality of this disease[10;11].

The need for OSA (and OHS) screening is still subject to discussion in many bariatric practices. Important reasons are limited sleep laboratory capacity, costs, time management and lack of high quality evidence showing the benefit of OSA screening and treatment in the bariatric population. In a systematic review on the OSA related outcome in bariatric surgery, OSA was not a risk factor for complications. This conclusion was based on level IV-V evidence including a high risk of selection bias i.e. no routine sleep studies for OSA diagnosis and optimized situations such as CPAP, opioid avoidance and continuous postoperative monitoring[12]. In a large cohort published hereafter, 1358 bariatric patients underwent mandatory sleep studies prior to surgery. Cardiopulmonary complications did not differ between OSA severity groups. As

other studies have found a higher incidence of complications in OSA patients, these results suggest that recognition and treatment of OSA results in a decrease of OSA related complications[13]. The lack of level I evidence could be explained by published meta-analyses reporting an increased perioperative risk in patients with OSA[14-16]. Performing studies in which all diagnosed OSA patients are randomized for OSA treatment or no treatment would be against ethical agreements. Another difficulty is the low complication rate, requiring a large sample size to detect a significant difference. Conclusions and recommendations are hence based on best available evidence i.e. large cohorts, experts' opinion and common sense.

Perioperative management; time to wake up

Ventilation strategies aim to minimize the risk of postoperative complications. CPAP is the first treatment choice for OSA and is recommended in all bariatric patients with moderately or severe OSA (AHI greater than 15/hour)[2]. CPAP significantly reduces the AHI and data is available suggesting a decreased risk of pulmonary complications, atelectasis and reintubation with CPAP initiation in the postoperative period following major abdominal surgery[9;17;18]. A recent systematic review reported that noninvasive pressure ventilation (NIPPV) in the immediate postoperative period decreased the risk of respiratory complications, incidence of postoperative hypertension, oxygen disturbances and prolonged stay in the post anesthesia care unit (PACU)[19]. NIPPV had no effect on number of reintubations or unplanned ICU admissions[19].

Which ventilation strategy i.e. CPAP or bi-level PAP (BPAP) is superior in the bariatric population is not clear. Both CPAP and BPAP showed beneficial effects, but there is a lack of comparative studies[7]. A recent randomized controlled trial found similar improvements of OHS with BPAP and CPAP[20]. These new study results are in line with our consensus recommendation to provide CPAP as standard treatment for OSA and OHS. For those with inadequate alveolar ventilation, BPAP could be considered. For both ventilation strategies, supplementary oxygen might be necessary for those with desaturations despite PAP therapy[2;11].

CPAP titration should follow as soon as possible after OSA diagnosis to enhance acclimatization before surgery. The choice of nasal or full face mask is based on comfort and compliance. When admitted to the hospital, patients should use their own CPAP mask and machine for optimal mask fit and pressure requirements[2].

Other intraoperative ventilation strategies include preoxygenation, positive end-expiratory pressure (PEEP) and low tidal volume. Optimal preoxygenation is achieved by placing patients in sitting position (90°). This extends time to apnea with one minute when compared with supine position[21]. The ramped position is the optimal position for induction, intubation and ventilation as this improves oxygenation and the laryngoscopic view[2]. The supine position should be avoided at all times. Videolaryngoscopy should be available for patients with an expected difficult intubation. Providing CPAP and PEEP during induction avoids airway collapse and increases end-expiratory lung volume. This combination extends time to hypoxic apnea by one minute, prolonging time for intuba-

tion[21]. High flow oxygen could be considered as adjuvant strategy to decrease time to desaturation during induction[2]. During the surgical procedure, maintenance of low tidal volumes reduces the risk of postoperative pulmonary complications[21].

Anesthesia and analgesia play an additional role in risk reduction and improvement of postoperative outcome. Early and full recovery of neuromuscular reflexes are important aspects of anesthesia and can be achieved by administering short acting agents[22]. Opioids should be avoided or used with caution as this induces respiratory depression and relaxation of the upper airway dilator muscle. At the same time, pain management is of essence to avoid a negative impact of pain on recovery, hemodynamics, respiratory status and length of hospital stay.

Multimodal anesthesia and analgesia include usage of several low risk drugs and plays an important role in reducing opioid administration and improving postoperative analgesia and outcome[22]. In an observational study of 412 bariatric patients, multimodal analgesia resulted in shorter PACU stay, lower postoperative opioid requirements, less postoperative vomiting, earliest oral intake and shorter hospital stay compared to unimodal morphine analgesia[23]. Choice of drugs as well as the use of appropriate dosing strategies are important considerations in this approach.

Pain management of bariatric patients with OSA is in line with the WHO pain ladder starting with paracetamol and NSAIDS[22]. Tramadol and opioids should be minimized and can be replaced by adjuvants to core analgesics including magnesium, ketamine, dexamethasone and clonidine/dexmedetomidine[2;22]. Also in adolescents, dexmedetomidine as adjuvant results in less opioid requirements after bariatric surgery[24]. Regional anesthesia for example with lidocaine has shown positive results and is recommended for all bariatric patients[2;22].

At the end of the surgical procedure, patients should be fully awake with reversed neuromuscular blockade prior to extubation[2]. CPAP usage in the direct postoperative period reduces the AHI and ODI by 69% and results in a higher oxygen saturation[2;25]. New data is available showing that CPAP mitigates respiratory depressant effects of opioids after bariatric surgery. In the group receiving oxygen with atmospheric pressure, opioids increased the AHI by 13%, from 28±32/hour to 32±58/hour. CPAP seemed to decrease this effect. With CPAP, the AHI increased from 6±11/hour by 4%, without affecting hemodynamics[25].

CPAP requirements may change in the postoperative setting and can be assessed by continuously monitoring vital signs and SaO_2[2]. As CPAP compliance is not guaranteed, all OSA patients should be continuously monitored in the early postoperative setting until they are no longer at risk for respiratory depression. The minimum required monitoring is with pulse oximetry[2].

Described strategies all fit in the enhanced recovery after bariatric surgery (ERABS) protocols which have become common practice in most bariatric clinics. The perioperative management of the bariatric patient including knowledge of OSA and OHS is displayed in **Figure 1**.

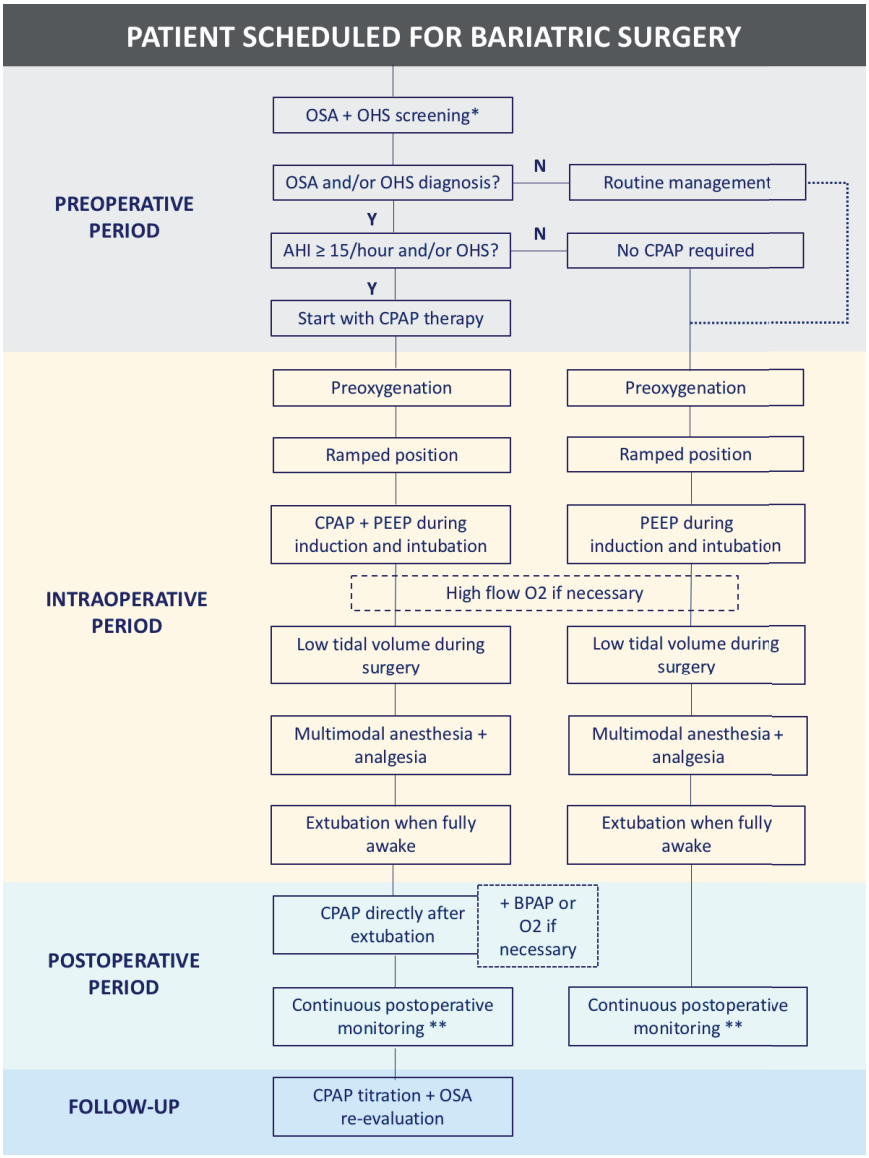

Figure 1 – Perioperative management of the bariatric patient with and without OSA
* OSA: sleep study (1st choice) or STOP-Bang/Berlin questionnaire (2nd choice); OHS: venous HCO_3^-
** Until patients are no longer at risk for respiratory depression
BPAP = Bilevel Positive Airway Pressure; CPAP = Continuous Positive Airway Pressure; OHS = Obesity Hypoventilation Syndrome; OSA = Obstructive Sleep Apnea; PEEP = Positive End-Expiratory Pressure

Follow-up

OSA patients using CPAP should be re-evaluated with a formal sleep study prior to the decision of discontinuing CPAP[2]. Optimal timing of this re-evaluation is unknown. Weight loss has been an important aspect in this decision making[2]. Recent data suggest the involvement of hormonal changes, directly occurring after bariatric surgery. Amin and colleagues performed a polysomnography in 7 OSA patients at three intervals: before and at three and five weeks after bariatric surgery. The AHI decreased by 9.2/hour after three weeks and 9.1/hour after five weeks ($p < 0.01$). There was no difference between three and five weeks postoperatively. Significant decrease of leptin and increase of orexin after three weeks. These results suggest that AHI changes are independently from weight loss[26]. Larger cohorts including multiple follow-up moments of sleep studies are required to recommend optimal timing of re-evaluation.

CONCLUSION

This review provided tools for the perioperative management of OSA patients undergoing surgery. Attention should be paid on the preoperative recognition of OSA and OHS. Intra-operative precautions are correct positioning of the patient, preoxygenation, administration of CPAP and PEEP during induction, maintenance of low tidal volume during surgery and performance of multimodal anesthesia and analgesia with avoidance of opioids. Extubation is considered safe when a patient is fully awake and should directly be followed by CPAP treatment. Continuous monitoring is recommended for all OSA patients in the early postoperative period.

Keypoints

- All bariatric surgery patients should be screened for OSA and OHS.
- CPAP is the first treatment choice for moderately and severe OSA and OHS; BPAP or supplemental oxygen can be considered in cases of inadequate ventilation or desaturation respectively.
- Intraoperative approaches are preoxygenation, ramped position, CPAP and PEEP during induction, supplemental high flow oxygen and maintaining low tidal volume.
- Multimodal analgesia with avoidance of opioids has shown beneficial results on postoperative outcome and plays an important role in the fast track protocol.

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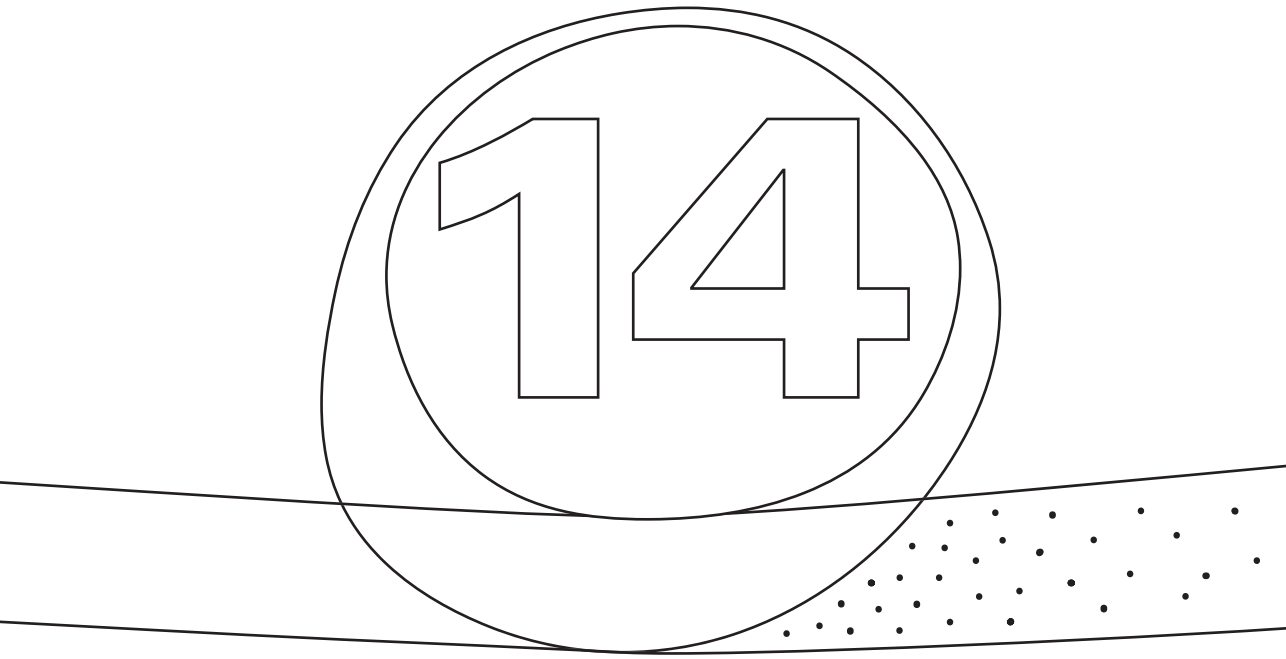
Discussion and future perspectives



DISCUSSION AND FUTURE PERSPECTIVES

Obstructive sleep apnea (OSA) is not a new disease by any means. Symptoms of OSA have been described nearly 2000 years ago. Before OSA was officially named and recognized as a disease, it was called Pickwickian syndrome. The name came from Charles Dickens' Pickwick papers, in which a person called Joe, a fat boy, had all classic symptoms of the condition that later would become known as OSA. Scientists who reviewed historical reports of persons and characters, believe that Napoleon Bonaparte, Johannes Brahms, Falstaff (Shakespeare) and Winston Churchill suffered from OSA as well[1].

In the twentieth century, OSA was recognized as a disease. The 1950s saw an uptake in apnea research and its relation with obesity was established soon[2]. A mere 300 articles appeared in medical literature in the period 1975-1980. Bariatric surgery for morbid obesity likewise developed in the late twentieth century. Surgical techniques, complications and weight control were main outcome measures at first. Interest in comorbidities, quality of life and Enhanced Recorvery After Surgery (ERAS) protocols followed rapidly. Topics on OSA in combination with bariatric surgery has caught the attention of many researchers and clinicians over the last 30 years. Publication numbers on this subject have increased from less than twenty in 1990 to more than 1000 in 2018.

This thesis aimed to provide more knowledge regarding the perioperative management of OSA in bariatric surgery. Findings of this thesis are applicable in current daily practice by the provided clinical recommendations and tools. This section includes discussion points and future perspectives for the existing obesity epidemic and its drastic effects in terms of OSA, surgical needs and following management.

Bariatric surgery was developed as a long-term treatment for morbid obesity. For those who failed conservative therapies, results in terms of weight loss, improvement of comorbidities and increasing life expectancy outweigh the risks of surgery[3]. Evolution of minimal invasive techniques and standardized care have led to a situation in which bariatric surgery has become reimbursed and common practice. Findings of several reports indicate a serious challenge for bariatric surgeons. Fifty-five million people are morbidly obese and are potential candidates for bariatric surgery worldwide. Assuming an average annual performance of 600.000 procedures, more than 90 years are required to surgically cure existing morbid obesity. Alarming reports of the continuous rise of overweight and obesity in children and adults predict a growth of morbid obesity[4]. In 2016, overweight and obesity affected 41 million children under the age of five years, 340 million children and adolescents aged 5-19 years and 1.9 billion adults aged 18 years and over[5]. Knowing that childhood obesity increases the risk of lifelong obesity, serious health problems and a reduction of life expectancy between ten and 20 years[6-7], a three folded prevalence of childhood obesity confirms the dramatic obesity crisis the world is dealing with in the 21st century. Bariatric surgery is no solution for this growth and governments, industries, local authorities

and the public should drastically come up with a plan to tackle the problem of obesity, a disease that is preventable.

For those in whom morbid obesity was not prevented and those who failed long-term weight loss by themselves, bariatric surgery could be an option. High volume centers including experienced surgeons and ERAS protocols contribute to standardized care and reduced complication rates. Clinical practices and this thesis underline the challenging task of OSA management in bariatric ERAS protocols. Doubts on the relevance of OSA in the perioperative setting are still existing and OSA recognition and risk reduction strategies are in conflict with strict time schedules to surgery, capacity and costs.

OSA patients undergoing any kind of surgery have an increased risk to develop cardiovascular and respiratory complications perioperatively[8]. This risk was not proven in the bariatric population (chapter 5), most likely due to the low occurrence of complications, absence of OSA severity notification and optimized situations such as usage of Continuous Positive Airway Pressure (CPAP), anesthetic care, continuous postoperative monitoring and admissions to the Intensive Care Unit (ICU). Finding the true magnitude of OSA related perioperative risks in bariatric surgery and the effect of strategies to decrease this risk requires randomized controlled trials in which all patients undergo polygraphy/polysomnography (PG/PSG) and diagnosed OSA patients are randomized to bariatric care plus OSA management or solely bariatric care. Practical implementations, however, are deal breaking. Low complication rates will require large sample sizes and ethical committees cannot possibly accept such studies in which patients are at risk of rare, but fatal outcomes. In line with obesity, why wait for serious complications to happen when they may be avoided.

OSA management in the bariatric population is not comparable to other OSA groups and deserves a special approach. Morbid obesity, OSA, surgery, enormous amount of weight - and hence apnea-hypopnea-index (AHI) loss, cost-efficiency and ERAS principles are all important components that should fit in one protocol.

Step-wise approaches including OSA screening and personalized medical care covering CPAP therapy, anesthetic care, postoperative monitoring and follow-up seem the most common and logical ones (chapter 12 and 13). High OSA prevalence (chapter 2 and 12) and the knowledge AHI decreases with weight loss have caused other bariatric clinics to follow opposite protocols assuming all bariatric patients might have OSA. In those clinics, postoperative vital parameters are continuously monitored at a designated surgical ward. OSA screening and therapy is not performed. The idea behind this approach is that any patient with undiagnosed OSA is monitored in the postoperative period and bariatric surgery will treat their OSA in the long term. Dutch studies are currently investigating which protocol benefits OSA related perioperative risks, quality of life (QoL) and cost-efficiency.

Another important consideration is to ascertain whether perioperative OSA strategies should be designed to exclusively decrease risks of OSA related perioperative complications, or to provide OSA therapy after hospital discharge as well. Reversed

anesthesia and absence of sedatives and opioids post-surgery reflect a OSA situation that is comparable to the preoperative situation at home. AHI reduction following weight loss (**chapter 11**) even improves the preoperative status and reduces long-term OSA related complications. Studies investigating the benefits of additional post-bariatric CPAP therapy in terms of QoL and long-term cardiovascular- and respiratory risks along with excessive weight loss have not been performed. Bariatric surgeons also wonder their responsibility in the management of pre-existing comorbidities such as OSA, other than in the direct related perioperative setting. When available in countries, there might be a role for general practitioners for routine OSA screening in morbidly obese patients. This will allow time to diagnosis and CPAP acclimatization, improvement of QoL and provision of information on OSA status if morbidly obese patients are scheduled for any type of surgery requiring sedatives or opioids.

Key points in this discussion are recognition of OSA, estimating related risks and anticipation to decrease perioperative adverse events. PSG/PG are the most reliable diagnostics to determine OSA severity to date (**chapter 2 and 12**). Performances of such formal sleep studies in bariatric patients are of clinical issue, due to a lack of capacity, delay to surgery and costs. Expected OSA improvement following weight loss additionally questions the importance of determining the exact AHI prior to bariatric surgery. Speaking in terms of reducing perioperative risks, estimating OSA severity and need for additional strategies might be enough.

Patients diagnosed with moderate and severe OSA, defined as an AHI ≥ 15/hour, are generally referred to the pulmonologist for CPAP. A test differentiating between those who do and do not require CPAP therapy might enable physicians to leave out PG/PSG and immediately start CPAP therapy. With this hypothesis to rule out PG/PSG, the value of the Checkme monitor was evaluated (**chapter 3**). Specificity was 69%, meaning that 31% of patients who are diagnosed with moderate or severe OSA actually have no or mild OSA and would incorrectly be referred for CPAP therapy. Patient burdensome, time to surgery and costs are reasons not to accept this percentage. Another important reason to search for alternatives is its inability to estimate severity, other than knowing a patients' AHI is ≥ 15/hour. Auto-PAP is a type of PAP therapy that is able to automatically adjust pressure along need and is applicable for any AHI level. One could wonder whether knowing the AHI provides extra therapeutic strategies when using auto-PAP. Large differences in AHI, CPAP compliance and efficacy, however, are essential components that bariatric care givers should be aware of. Poor CPAP compliance and efficacy are recognized problems in OSA patients. Difficult mask fit, noise, social bed problems and adverse events such as mask irritation all contribute to these low compliance rates. Information on compliance might be very relevant for further decision making. Patients with an AHI of 15/hour intuitively require another approach than patients with an AHI of ≥120/hour. Poor compliance and/or efficacy rates in both groups might result in continuous monitoring on a surgical ward for the first group and comprehensive ICU monitoring for the latter. Nearly 6% of bariatric patients have an AHI ≥ 60/hour; 1.3% an AHI ≥

90/hour. Number needed to screen to find these patients are 18 and 77 respectively (**chapter 7**). Screening tools including additional severity categories on top of AHI ≥ 15/hour and ≥ 30/hour seem of clinical value and create potential for biomarkers and wearables providing continuous outcomes.

Finally, results of this thesis are meant to create awareness, provide multiple clinical tools to decrease risks of OSA, and make room for a period of excessive weight loss, reduction of AHI and improvement of QoL. Results have been shared during bariatric and OSA related congresses and courses and will soon be published in an OSA text book.

Impressive postoperative results and the increasing prevalence of obesity predict a further growth in bariatric performances worldwide. The areas of clinical care where there is paucity of evidence, which is particularly true in the case of OSA in bariatric surgery, should challenge physicians and researchers to perform further research and optimize bariatric care.

Instead of holding on to an unknown and perhaps high number to treat, physicians should examine easy, low-cost, patient friendly and worldwide applicable tools to recognize OSA related risks, and with low efforts decrease the risk of potential, preventable fatal outcomes.

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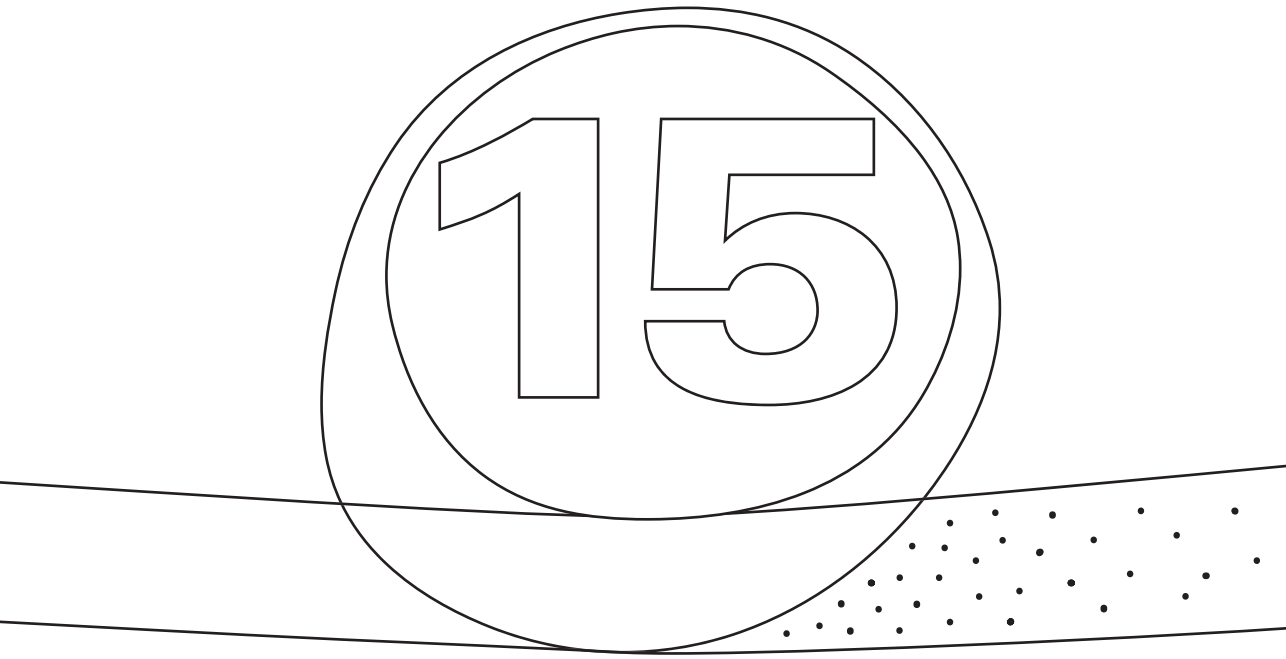
English summary



THESIS SUMMARY

Studies enclosed in this thesis focused on the perioperative setting of obstructive sleep apnea (OSA) patients undergoing bariatric surgery. Special attention was paid on OSA screening and diagnosis, perioperative risks as well as clinical strategies to optimize perioperative care, and postoperative outcomes such as weight loss and improvement or curation of OSA. This chapter provides an overview of main findings.

In **chapter 2**, the true prevalence of OSA with respect to different severity levels was determined in patients undergoing bariatric surgery. Data on the number of upper airway collapses per hour during sleep i.e. the apnea-hypopnea index (AHI) were retrospectively collected from polysomnography (PSG) sleep studies that are considered the gold standard to diagnose OSA. Out of 1358 included patients in whom preoperative PSG were routinely performed, two-third suffered from OSA (AHI ≥ 5/hour). One-third was even diagnosed with a moderate (AHI 15-30/hour) or severe form (AHI ≥ 30/hour).

In **chapter 3** and **4,** the validity of other OSA diagnostics were assessed by comparing results with the gold standard. In **chapter 3** the value of venous derived biomarkers and the validity of a prediction model as a screening tool for OSA in bariatric surgery were analyzed. In this prospective study of 126 patients, OSA was diagnosed by PSG in 57.9%. The optimal prediction model included plasminogen activator inhibitor-1, angiopoietin-like protein 7 and Tumor necrosis factor-alpha. This model is not accurate to replace PSG due to wide confidence intervals, but can be used to rule out moderate or severe OSA in 23% of patients and withhold them from preoperative PSG. In **chapter 4,** the validity of a simple sleep monitor called the Checkme Health Monitor was evaluated by assessing the diagnostic performance of the Checkme derived oxygen desaturation index (ODI) for PSG AHI ≥ 15/hour. With a sensitivity and negative predictive value of both 100%, the Checkme is valid for exclusion of moderate and severe OSA in bariatric surgery. This simplified sleep study enables bariatric clinics not to perform PSG in all patients scheduled for bariatric surgery.

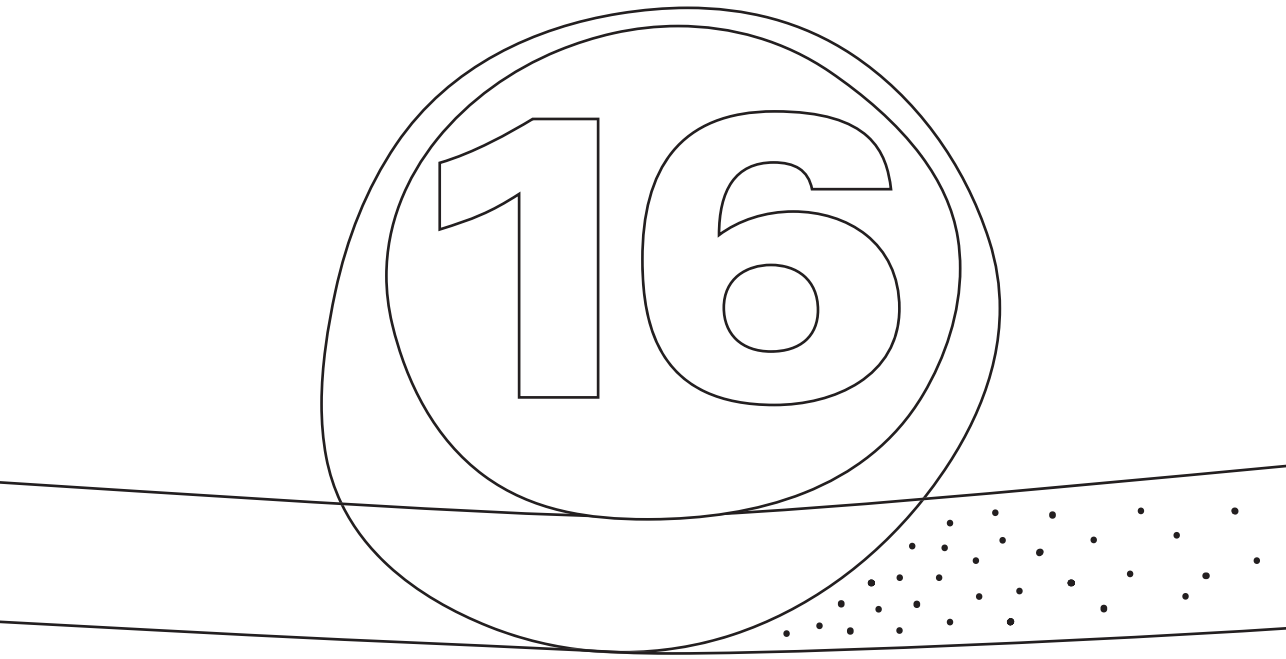
Subsequent two chapters focused on the association of postoperative cardiopulmonary complications and OSA in bariatric surgery patients. **Chapter 5** presents a systematic review of the literature and included thirteen studies providing 98,935 patients. Overall presented data showed no clear association of OSA with cardiopulmonary morbidity, admissions to the Intensive Care Unit (ICU), mortality or length of stay after bariatric surgery. Important notes are the under diagnosis of OSA with only 37% patients documented with OSA and high risk of bias caused by optimized conditions such as continuous positive airway pressure (CPAP) usage, continuous monitoring of vital parameters and oxygen supplementation. The need of CPAP usage in mild OSA patients (AHI 5-15/hour) who are positional (POSA), meaning that their AHI is at least twice as high in supine sleeping position than in other positions,

was investigated in **chapter 6**. Out of 277 mild OSA patients, 153 (55%) had POSA. Severe cardiopulmonary complications occurred in 1.1% of mild OSA patients. No difference was detected between POSA and non-POSA patients. Results of this study suggest that CPAP is not indicated in mild OSA patients, despite existence of a positional component.

The following four chapters evaluated the influence of OSA on bariatric surgical outcomes including anastomotic leakage, weight loss and quality of life (QoL). The association of perioperative CPAP usage, possibly predisposing to mechanical stress by increased air pressure in esophagus and stomach, and the risk of suture line disruption after bariatric surgery was assessed in **chapter 7**. A total of 2135 patients were included; 497 (23%) used CPAP postoperatively. Suture line disruption occurred in 1.2% and was not associated with CPAP usage. This study concluded that CPAP usage is safe in the early postoperative setting of bariatric surgery. In **chapter 8**, the influence of the AHI on 30-day complications including severity measured by the Clavien-Dindo classification was explored. Retrospective analyses of 1002 patients showed no effect of the AHI on short-term complications. In **chapter 9**, one-year weight loss results were compared between different OSA severity levels. Less percentage excess weight loss (EWL) was seen with increasing AHI. However, when adjusted for other OSA related factors, the AHI was of minor importance. It was concluded that the AHI itself does not individually impair weight loss after bariatric surgery. Additionally, the influence of OSA on QoL prior to- and after laparoscopic Roux-en-Y gastric bypass surgery was examined by using the Impact of Weight on QoL-Lite questionnaire (**chapter 10**). Total scores (n=276) improved from 51.2 to 89.7. QoL improved in both OSA and non-OSA groups. Lower postoperative scores of subscales Public Distress and Work were observed in OSA patients, especially those with a severe form. All postoperative subscale scores were negatively correlated with OSA severity. In **chapter 11**, the effect of weight loss following bariatric surgery on OSA improvement in terms of CPAP dependency was evaluated. Out of 205 patients with preoperative moderate and severe OSA (AHI ≥ 15/hour), three quarter achieved curation or improved from severe or moderate OSA to a mild form of OSA after surgical induced weight loss. A quarter (25.9%) had persistent moderate or severe OSA. Predictive factors for this persistence were age ≥ 50 years, preoperative AHI ≥ 30/hour, EWL < 60% and hypertension.

Chapter 12 outlines a consensus based guideline on the perioperative management of OSA in a bariatric specific population. After systematic literature searches, a panel of 15 international experts provided 58 recommendations or statements covering preoperative screening, treatment, postoperative monitoring, anesthetic care and follow-up. This was done according to the "Amsterdam Delphi method". With the exception of 3 recommendations (64%, 66%, and 66% respectively), consensus (>70%) was reached for 55 statements and recommendations. **Chapter 13** provides a summary and update on **chapter 12**, one year after publication.

Nederlandse samenvatting



NEDERLANDSE SAMENVATTING

Studies in dit proefschrift hebben zich gefocust op het perioperatieve traject van patiënten met obstructief slaap apneu (OSA) die bariatrische chirurgie ondergaan. Speciale aandacht werd besteed aan OSA screening en diagnostiek, de perioperatieve risico's evenals klinische strategieën om de perioperatieve zorg te optimaliseren, en postoperatieve uitkomsten zoals gewichtsverlies en verbetering of genezing van OSA. Dit hoofdstuk geeft een overzicht van de hoofdbevindingen.

Hoofdstuk 2 geeft de prevalentie van OSA weer, inclusief de verschillende ernst classificaties, bij patiënten die bariatrische chirurgie ondergaan. Data aangaande het aantal collapsen van de bovenste luchtweg per uur gedurende de slaap, ook wel de apneu-hypopneu-index (AHI) genoemd, werden retrospectief verzameld van polysomnografie (PSG) slaap studies die worden beschouwd als de gouden standaard om OSA te diagnosticeren. Van de 1358 patiënten bij wie preoperatieve PSG routinematig werd verricht, bleek twee-derde OSA (AHI ≥ 5/uur) te hebben. Een-derde werd zelfs gediagnosticeerd met een matige (AHI 15-30/uur) of ernstige (AHI ≥ 30/uur) vorm.

Hoofdstuk 3 en 4 behandelen de validiteit van andere OSA diagnostica door deze te vergelijken met de gouden standaard. Hoofdstuk 3 bevat analyses over de waarde van veneus verkregen biomarkers en de validiteit van een predictiemodel als screeningsinstrument voor OSA bij bariatrische chirurgie. In deze prospectieve studie van 126 patiënten werd OSA door middel van PSG gediagnosticeerd bij 57,9%. Het meest optimale predictiemodel bevatte de biomarkers 'plasminogen activator inhibitor-1', 'angiopoietin-like protein 7' en 'tumor necrosis factor-alpha'. Dit model is niet accuraat genoeg om de PSG te vervangen in verband met brede betrouwbaarheidsintervallen, maar kan wel gebruikt worden om matig en ernstig OSA bij 23% van de patiënten uit te sluiten en hen daarmee te weerhouden van preoperatieve PSG.

In hoofdstuk 4 wordt de validiteit van een simpele slaapmonitor genaamd de "Checkme Health Monitor" geëvalueerd door de diagnostische waarde te beoordelen van de door Checkme verkregen zuurstofdesaturatie-index voor de PSG verkregen AHI ≥ 15/uur. Met een sensitiviteit en negatief voorspellende waarde van beide 100%, is de Checkme valide om matig en ernstige OSA te excluderen bij bariatrische chirurgie. Deze gesimplificeerde slaapstudie kan voorkomen dat PSG in alle bariatrische patiënten moet worden verricht.

De volgende twee hoofdstukken richten zich op de associatie tussen OSA en postoperatieve cardiopulmonale complicaties bij patiënten die bariatrische chirurgie ondergaan. Hoofdstuk 5 beschrijft de resultaten van een systematische review van de literatuur waarbij er dertien studies, en daarmee 98.935 patiënten, zijn geïncludeerd. Over het totaal genomen was er geen duidelijke associatie tussen OSA en cardiopulmonale complicaties, opnames op de Intensieve Zorg afdeling, mortaliteit of opname duur na bariatrische chirurgie. Belangrijke aantekeningen zijn de onder

diagnostiek van OSA waarbij slechts bij 37% OSA werd gedocumenteerd en het hoge risico op bias door geoptimaliseerde condities zoals het aanbieden van continue positieve luchtweg druk (CPAP) therapie, continue monitoring van vitale parameters en zuurstofsuppletie. In **hoofdstuk 6** wordt de waarde van CPAP onderzocht bij lichte OSA patiënten (AHI 5-15/uur) die positionele OSA (POSA) hebben. Bij hen is de AHI minstens twee keer zo hoog in rugligging dan in andere posities en zou er wellicht een indicatie zijn voor CPAP therapie. Van de 277 lichte OSA patiënten, hadden er 153 (55%) POSA. Ernstige cardiopulmonale complicaties traden op bij 1.1% van de totale studiepopulatie. Er was geen verschil tussen patiënten die wel en geen POSA hadden. Resultaten van deze studie geven de suggestie dat aanwezigheid van POSA bij lichte OSA-patiënten geen indicatie is voor CPAP therapie.

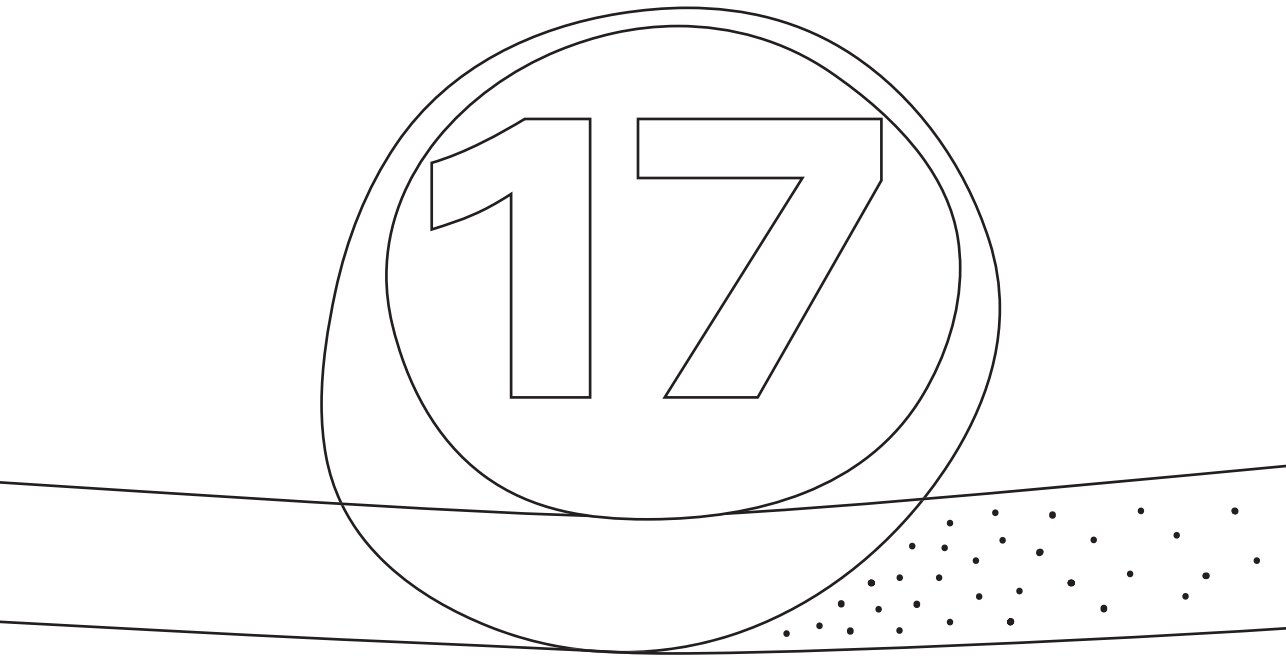
De volgende vier hoofdstukken hebben gekeken naar de invloed van OSA op bariatrische uitkomsten zoals naadlekkage, gewichtsverlies en kwaliteit van leven. In **hoofdstuk 7** werd gekeken naar de associatie tussen perioperatief CPAP gebruik, wat mogelijk predisponeert voor mechanische stress door een verhoogde luchtdruk in de oesofagus en maag, en het risico op naadlekkage na bariatrische chirurgie. In totaal werden 2135 patiënten geïncludeerd; 497 (23%) van hen maakten postoperatief gebruik van CPAP. Naadlekkage trad op bij 1,2% en was niet geassocieerd met gebruik van CPAP. Deze studie concludeerde dat CPAP gebruik veilig is in de eerste postoperatieve fase na bariatrische chirurgie.

Hoofdstuk 8 focust zich op de invloed van de AHI op het optreden van korte termijn (binnen 30 dagen) complicaties inclusief de verschillende ernstclassificaties volgens de Clavien-Dindo. Retrospectieve analyse van 1002 patiënten liet geen effect zien van de AHI op korte termijn complicaties. In **hoofdstuk 9** wordt het gewichtsverlies één jaar na chirurgie vergeleken tussen de verschillende OSA ernst klassen. Hoe hoger de AHI, hoe minder percentage verlies van het overtollige gewicht er werd gezien. Na correctie voor andere OSA gerelateerde factoren, had de AHI zelf echter weinig invloed. Er werd geconcludeerd dat de AHI individueel niet voor minder gewichtsverlies zorgt na bariatrische chirurgie. **Hoofdstuk 10** toont een overzicht van de invloed van OSA op de kwaliteit van leven voor en na laparoscopische Roux-en-Y gastric bypass chirurgie door gebruik te maken van de 'Impact of Weight on Quality of Life-Lite' (IW-QoL) vragenlijst. Totale scores (n=276) verbeterden van 51,2 naar 89,7. De kwaliteit van leven verbeterde zowel bij patiënten met- en zonder OSA. Lagere postoperatieve scores voor de subschalen 'Public Distress' en 'Work' werden geobserveerd bij OSA patiënten, met name bij degenen met een ernstige vorm. Alle postoperatieve subschaal scores lieten een negatieve correlatie met de OSA ernst zien. In **hoofdstuk 11** werd gekeken naar het effect van gewichtsverlies na bariatrische chirurgie op OSA verbetering in termen van CPAP afhankelijkheid. Van de 205 patiënten die preoperatief een matig of ernstige vorm van OSA hadden (AHI ≥ 15/uur), bereikte driekwart curatie (AHI < 5/uur) of verbetering naar een lichte vorm van OSA (AHI 5-15/uur) na chirurgie geïnduceerd gewichtsverlies. Een kwart (25,9%) had persisterend matig of ernstige OSA. Voorspellende factoren hiervoor waren leeftijd ≥

50 jaar, preoperatieve AHI ≥ 30/uur, hypertensie en minder dan 60% verlies van het overtollig gewicht.

Hoofdstuk 12 geeft een op consensus gebaseerde richtlijn weer over de perioperatieve zorg van OSA bij bariatrische chirurgie. Na systematische literatuurzoekacties heeft een panel van vijftien internationale experts 58 aanbevelingen en uitspraken geformuleerd over preoperatieve screening, behandeling, postoperatieve monitoring, anesthesiologische zorg en follow-up. Dit werd gedaan volgens de "Amsterdam Delphi methode". Met uitzondering van 3 aanbevelingen (respectievelijk 64%, 66% en 66%), werd consensus (>70% overeenkomst tussen experts) bereikt voor 55 aanbevelingen en uitspraken. Hoofdstuk 13 presenteert een samenvatting en update van hoofdstuk 12, één jaar na publicatie.

List of publications
PhD portfolio
Curriculum Vitae
Dankwoord



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Other publications: contribution to textbook

2019 Current Concepts in Sleep Surgery (Verse & de Vries)
Chapter 9: Bariatric surgery + Chapter 10.2: Perioperative Management: Surgeons' Perspective

PhD PORTFOLIO

PhD period: jun 2014- feb 2019
PhD supervisors: Dr. B.A. van Wagensveld, Prof. dr. N. de Vries, Prof. dr. H.J. Bonjer

	Year	APH accreditation (ECTS)
General courses		
BROK (Basiscursus Regelgeving Klinisch Onderzoek)	2014	1,5
Scientific writing	2014	2
Scientific integrity	2016	2
Clinical prediction models	2016	2
Missing data: consequences and solutions	2016	2
Epidemiologisch onderzoek: opzet en interpretatie	2016	4
Seminars/meetings		
Refereeravonden en intercollegiale overleggen (>15x)	2014-2018	2
Meetings sharing bariatric expertise (>3x)	2015-2017	1
International oral presentations		
Obstructive sleep apnea meeting, Zagreb, Croatia	2018	2
9th International Surgical Sleep Society Meeting, Munich, Germany	2018	2
Ear-Nose-Throat World Congress, Paris, France	2017	2
European Obesity Summit 2016, Gothenburg, Sweden	2016	2
21th World Congress of International Federation for the Surgery of Obesity & Metabolic Disorders, Rio de Janeiro, Brazil	2016	2
20th World Congress of International Federation for the Surgery of Obesity & Metabolic Disorders, Vienna, Austria	2015	2
National oral presentations		
Lustrumcongres Nederlandse Vereniging voor Tandheelkundige Slaapgeneeskunde, Amsterdam	2018	1
Nederlandse Vereniging voor Keel-Neus-Oorheelkunde en Heelkunde van het Hoofd-Halsgebied, Nieuwegein	2017	1
Landelijke refereermiddag Keel-Neus-Oorheelkunde, Amsterdam	2017	1
Dutch Society for Metabolic and Bariatric Surgery, Doorn	2017	1
Round table bariatrie, Rotterdam	2017	1
SLAAP congres, Ermelo	2016	1
24th International congress of the European Association of Endoscopic Surgery, Amsterdam	2016	1
Wetenschapsdag OLVG, Amsterdam	2016	1

	Year	APH accreditation (ECTS)
Nederlandse Vereniging van Artsen voor Longziekten en Tuberculose, Utrecht	2016	1
Symposium "OSA revisited", oration Prof. dr. N. de Vries, Amsterdam	2016	1
Dutch Society for Metabolic and Bariatric Surgery (DSMBS), Doorn	2016	1
Regiobijeenkomst NL apneu vereniging	2016	1
Wetenschapsdag OLVG, Amsterdam	2015	1
Dutch Society for Metabolic and Bariatric Surgery (DSMBS), Doorn	2015	1
Heelkunde Regio 1 VUmc Wetenschapsdag, Amsterdam	2015	1
Noord-Hollands Pulmonologisch Genootschap, Amsterdam	2015	1
Poster presentations		
22nd World Congress of International Federation for the Surgery of Obesity & Metabolic Disorders (IFSO), London, England	2017	2
Anesthesiology annual meeting, ASA, Chicago, USA	2016	2
European Obesity Summit 2016 (IFSO-European Chapter), Gothenburg, Sweden	2016	2
21th World Congress of International Federation for the Surgery of Obesity & Metabolic Disorders (IFSO), Rio de Janeiro, Brazil	2016	2
20th World Congress of International Federation for the Surgery of Obesity & Metabolic Disorders (IFSO), Vienna, Austria	2015	2
(Inter)national conferences		
23rd World Congress of International Federation for the Surgery of Obesity & Metabolic Disorders (IFSO), Dubai, United Arab Emirates	2018	1
NvVH, Veldhoven	2018	1
NvVH, Najaarsdag, Veldhoven	2018	1
OSA meeting, Kuwait city, Kuwait	2017	1
NvVH, Veldhoven	2015	1
NvVH, Najaarsdag, Veldhoven	2015	1
Wetenschapsdag OLVG, Amsterdam	2014	1
NvVH, Veldhoven	2014	1
NvVH, Najaarsdag, Veldhoven	2014	1
IFSO-EC, Bruxelles, Belgium	2014	1
Dutch Society for Metabolic and Bariatric Surgery (DSMBS), Doorn	2014	1
Frankfurter meeting, Frankfurt, Germany	2014	1

	Year	APH accreditation (ECTS)
Other		
Chairman organizing committee: international expert meeting "Perioperative care of obstructive sleep apnea in bariatric surgery"	2016	2
Moderator organizing committee: international expert meeting "Perioperative care of obstructive sleep apnea in upper airway surgery"	2018	2
Author of two textbook chapters	2018	-
Teaching		
Tutoring medical students (DM Bindt, AS Pierik, MC Kalff)	2015-2017	3
Total ECTS	2014-2019	73,5

CURRICULUM VITAE

Christel de Raaff werd geboren op 28 april 1989 in Amstelveen. Vanaf 2007 studeerde zij Geneeskunde aan de Vrije Universiteit van Amsterdam. Gedurende haar studie was zij in 2009 lid van het bestuur van de medische faculteitsvereniging (MFVU). Na het behalen van haar artsexamen in mei 2014 begon zij in juli, onder begeleiding van Dr. B.A. van Wagensveld, Prof. dr. N. de Vries en Prof. dr. H.J. Bonjer, met het onderzoek dat heeft geleid tot dit proefschrift. In het kader van haar onderzoek was zij in 2016 organisator en voorzitter van de eerste internationale consensus meeting over de perioperatieve zorg van obstructief slaap apneu bij bariatrische chirurgie. Zij werkte vervolgens als arts-assistent op de afdeling Heelkunde van het Onze Lieve Vrouwe Gasthuis, locatie West (dr. B.C. Vrouenraets & dr. M. Gerhards). In juli 2017 is zij begonnen met de opleiding tot chirurg in het Albert Schweitzer Ziekenhuis (dr. P.W. Plaisier).

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De leden van de leescommissie en oppositie, Prof. dr. G. Kazemier (Amsterdam Universitair Medische Centra, locatie VU Medisch Centrum), Prof. dr. M.W.M. van den Brekel (Antoni van Leeuwenhoek), Prof. dr. P.J. Wijkstra (Universitair Medisch Centrum Groningen), Prof. dr. J. de Lange (Amsterdam Universitair Medische Centra, locatie AMC), Prof. Dr. E.J. Hazebroek (Rijnstate) en Prof. S.G. Mattar (Oregon Health & Science University, Portland, Oregon, USA). Dank voor het beoordelen van dit proefschrift en de bereidheid zitting te nemen in mijn promotiecommissie. Dear Samer, it has been an honor and pleasure working with such a kind and inspiring person.

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